THE WOLFF-PARKINSON-WHITE AND RELATED SYNDROMES:

AN ELECTROCARDIOGRAPHIC APPRAISAL

By

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SECTION A

THE PRE-EXCITATION SYNDROMES

CHAPTER 1

Introduction

Nearly 60 years before this thesis is presented, and less than a decade after electrocardiography became established as a diagnostic technique, the first case of the Wolff-Parkinson-White syndrome was recognized. Identification of it as an example of the subject to be discussed in this thesis was retrospective, but re-examination of this first paper by Wilson (1915) shows that many of the cardinal features were present, and recognized by the author. These included the shortening of the P-R interval, with widening of the QRS complex, and tendency for these appearances to be unstable and to vary in relation to changes in vagal tone. Not only this: the first patient suffered from paroxysmal tachycardia and this was shown to be associated with a radical alteration in the form of the QRS complex, in that during the arrhythmia it became narrow and appeared of normal configuration.

It is not proposed to list the subsequent reports that appeared prior to the classical paper by Wolff et al. (1930); suffice it to say that several isolated case reports appeared that were subsequently recognized as representing this syndrome, including those of Wedd (1921) and Hamburger (1929).

The importance of the publication by Wolff et al. (1930) was that they collected, jointly from London and Boston, 11 patients who showed the electrocardiographic features of a short P-R interval and a broad QRS complex; and that they recognized that, apart from attacks of paroxysmal tachycardia, their patients, who were relatively young, were healthy. At first it was thought that the broadening of the QRS represented a form of bundle branch block, but it did not take long before it was recognized that this was not so, and for alternative explanations to be developed to explain the appearances (Holzmann and Scherf, 1932; Wolferth and Wood, 1933). The possibility of bundle branch block nevertheless remained in the minds of at least one of the original authors, although he recognized that it was apparent rather than real, when he collaborated in a further paper on this subject (Hunter et al., 1940).

Since the paper by Wolff et al. (1930) there have not only been numerous case reports, and papers on different aspects of the syndrome, but also a number of valuable reviews which have summarized the situation from time to time, and reference will be made to these in the course of this thesis.

Of particular value, giving one, so to speak, the opportunity to assess what was thought about it at those particular stages, were the surveys of Öhnell (1944), Scherf and Cohen (1964) and Chung et al. (1965); and more recently, and indeed, providing provocative challenges, is the far-ranging review by James (1970). Other useful surveys are those of Ferrer (1967), Durrer et al. (1970) and Wallace et al. (1971), and to these must be added the attempt to define the disturbance in the Wolff-Parkinson-White and related syndromes more closely by Castellanos et al. (1971a).

So much work having been done on this and related syndromes, so many papers having appeared, what justification can be offered for this thesis? Here an attempt will be made not only to review what has already been done, but to analyse the material available for study, and to look critically at some hypotheses about the nature of these syndromes. It is proposed to explore not only the nature of the Wolff-Parkinson-White and related syndromes, but also to look at other disorders in which some of the features may occur, in some of which indeed the Wolff-Parkinson-White syndrome may be brought to light. By "related syndromes" are meant those disorders that appear to be similar in origin, and also those that mimic it: that may masquerade as the Wolff-Parkinson-White syndrome. This is an electrocardiological study, based on electrocardiographic analysis of new cases as well as on a review of some features, hitherto unrecognized or not stressed, in subjects with these disorders, that may help throw more light on them. In six cases studied personally using intracardiac electrography - the technique of His bundle electrography - the contribution and relevance of this method will be analysed, and the results compared with the conclusions drawn from other contemporary work in this field. Thus, the clinical presentation of the cases, and of these syndromes, receives secondary attention, and more detailed analysis only when appropriate to substantiate the main burdens of the thesis. These case reports appear separately in Section C.

The mechanism of production of arrhythmias is becoming much better understood, and some of the diagnostic measures that are discussed in this work provide a clearer picture of their genesis. It is not proposed to embark upon a detailed consideration of anti-arrhythmic therapy in these syndromes, but the general principles will be discussed, and special reference will also be made to some new developments in this field.

The term "Wolff-Parkinson-White syndrome" will be used to define those cases showing the classical appearances of short P-R interval, wide QRS complex, and ST-T changes, of the type originally reported by Wolff et al. (1930), and that may or may not vary in electrocardiographic presentation from time to time, as discussed in Chapter 3. The term "Lown-Ganong-Levine syndrome" will be confined to cases in which the P-R interval is short (0.11 secs or less) but in whom the QRS complex is normal. The term "pre-excitation" (Öhnell, 1944) will be used where a portion of a ventricle receives the impulse generated supraventricularly, sooner than could occur were the impulse to traverse normal pathways in a physiological manner, and covers both syndromes. As is so often the case in Medicine, these definitions do not indicate water-tight compartments, and the question of differences of expression and reasons for modifications of the criteria will be explored.

CHAPTER 2

The Role of the Conduction Pathways

It is not proposed, save as it may prove relevant to the analysis of the pre-excitation and related syndromes, to review in detail the normal anatomical pathways for atrioventricular conduction in the human heart; excellent accounts of this appear in the publications of James (1963, 1970), Rosenbaum et al. (1970) and Schamroth (1971a). A brief survey of some aspects (Krikler, 1971a) will form the basis for discussion at a later stage. Suffice it to say that impulses normally originate at the sinoatrial node and are conducted to the atrioventricular node by specialized pathways; that in the atrioventricular node, these are transmitted downwards; and that they reach the ventricular myocardium via the bundle of His, the right and left bundle branches, and the terminal ramifications of these last structures. Pre-excitation, as already defined, indicates premature activation of a part of a ventricle, before the impulse could normally have arrived if conducted entirely down the normal pathways by physiologically normal processes. Whether structurally or functionally, an anomalous pathway provides the most realistic explanation for this phenomenon. Tracts that may possess this property thus deserve careful scrutiny.

When the normal pathways carry the impulse without interruption, the electrocardiogram shows conventional appearances, with a normal P-R interval, exceeding 0.12 seconds; a narrow QRS (usually less than 0.08 seconds); an iso-electric ST segment; and an upright T wave as the rule in all leads other than aVR (though it is often negative in V1 and may be so in some others, e.g. lead III). The normal P-R interval represents two activities: conduction from the sinoatrial node to the atrioventricular node, and conduction through the atrioventricular node to the bundle of His (Roberge et al., 1968). James (1963) has described three connecting pathways between sinoatrial and atrioventricular nodes and it is their behaviour that determines the major expression of the P-R interval. These contain Purkinje cells and myocardial fibres. The anterior and middle internodal tracts enter the highest part of the atrioventricular node, while the posterior internodal tract leaves the posterior margin of the sinoatrial node and runs to the posterior margin of the atrioventricular node, most of its fibres bypassing the atrioventricular node. The posterior internodal tract is often called the James tract or fibres. According to Sherf and James (1969), the normal stimuli descend in the anterior and middle internodal tracts, which are shorter, and thus the impulses arrive earliest at the crest of the atrioventricular node, producing a wave of depolarization parallel[1] to its long axis. These having thus depolarized the atrioventricular node, stimuli arriving later via the posterior internodal tract, which is longer, will find the atrioventricular node refractory, and they will thus be cancelled.

The classical appearances of the Wolff-Parkinson-White syndrome are demonstrated in a number of electrocardiograms in this work, and will be illustrated as appropriate. The cardinal features by which the syndrome is recognized consist of shortening of the P-R interval, widening of the QRS complex, deformity of the initial part of the QRS complex, and changes in the ST segments and T waves. These appearances can all be explained by the same basic mechanism, and the reasons for them are illustrated in Figure 1. The sinus impulse is conducted down both the normal and the anomalous pathways, and enters these tracts simultaneously. However, the anomalous pathway conducts the impulse more rapidly than does the normal pathway. Consequently, the impulse reaches the ventricles earlier than that part travelling down the atrioventricular node and the bundle of His. This results in the early inscription of the QRS complex. For this reason, the P-R interval is shortened. The area of myocardium initially reached by the impulse is not the specialized conducting tissue, but ordinary myocardium, which is a poor conducting medium. Conduction is therefore slower than normal, and the QRS complex has an initial deflection that is distorted and slurred: it has been called the delta wave (Segers et al., 1944), though Scherf and Cohen (1964) point out that it more closely resembles the Greek letter lambda. Its characteristics have been clearly defined by Schamroth (1971a). It is usually 0.04-0.06 seconds in duration, but it may be wider than this, and it may sometimes be higher than the succeeding QRS complex (Scherf and Cohen, 1964). It is usually upright when the QRS complex is mainly upright; the converse likewise applies, but when a negative delta is succeeded by an R wave, it may simulate the pathological Q wave of cardiac infarction.

When that part of the impulse travelling through the atrioventricular node in normal fashion reaches the ventricles, further transmission is through the normal conducting system, and takes place more rapidly. The area of depolarization in the ventricle, initiated by the anomalous pathway, has produced an impulse which fuses with that portion travelling down the normal pathways, and we then see the typical fusion complex of the Wolff-Parkinson-White syndrome. In the same way as depolarization is initiated in an irregular fashion, so is repolarization; hence the disturbance of the ST segments and T waves.

It was not long after the Wolff-Parkinson-White syndrome was recognized as a clinical entity by the workers with whose names the disorder is now associated, that others suggested an anatomical basis for its occurrence. Reference to the original report by Holzmann and Scherf (1932) reveals that they, within two years of the publication of the paper by Wolff et al. (1930), postulated that the muscular bundles linking atrium and ventricle on the right side of the heart (Kent, 1893;

1914) could be responsible for the appearances seen. In his papers Kent had erroneously proposed that these bundles were responsible for normal atrioventricular conduction; indeed, Paladino (1914) appears to have described these bundles as early as 1876. Almost simultaneously with Holzmann and Scherf (1932), Wolferth and Wood (1933) offered the same suggestion; they went slightly further in postulating that the paroxysmal tachycardia associated with the Wolff-Parkinson-White syndrome could be the result of retrograde conduction up the bundle of Kent. These remained theoretical, albeit very plausible, explanations for the Wolff-Parkinson-White syndrome, until some 10 years later, when Wood et al. (1943) reported the case of a boy who died at the age of 16 from paroxysmal tachycardia. The Wolff-Parkinson-White syndrome had been found on electrocardiogram two years previously when he presented with paroxysmal tachycardia. Examination of his heart revealed, on gross and histological study, three muscular connections at the right lateral border of the heart, between the right atrium and the right ventricle. Two of these bridged a small part of the right ventricular cavity in their course. The following year Öhnell (1944) reported a fatal case of the Wolff-Parkinson-White syndrome, in whom such connections were found on the left side of the heart. A fundamental physiological experiment that lent support to the proposition that a functioning bypass was responsible for the Wolff-Parkinson-White syndrome was the work of Butterworth and Poindexter (1942, 1944). These workers were able to reproduce on the electrocardiogram appearances of the Wolff-Parkinson-White syndrome by setting up an electrical connection between the atrium and the ventricle in the cat heart.

At this stage, the primacy, if not the uniqueness, of the bundle of Kent as <u>the</u> mechanism for the Wolff-Parkinson-White syndrome seemed to have been established. However, others have postulated a variety of different explanations, so that, eight years ago, Scherf and Cohen (1964) could indicate that at least 60 possible explanations for this syndrome had been advanced. It is not within the scope of this thesis to analyse all of these, but rather to review the most important ones on the basis of modern knowledge, and to show whether or how they can be linked with the Wolff-Parkinson-White and related syndromes.

The first soundly-based alternative anatomical pathway to be demonstrated consists of the paraspecific fibres of Mahaim (Mahaim and Winston, 1941; Mahaim, 1947). These are muscular strands that may arise, superiorly, from the atrioventricular node, bundle of His or proximal bundle branches, and that end in the myocardium of the interventricular septum. The frequency with which they can be demonstrated declines with age, and they are most commonly detectable in the very young (Davies, 1971); indeed, accessory atrioventricular muscle bundles appear to be common below the age of six months, and rare thereafter (Truex et al., 1958). It seemed possible that some aspects of the Wolff-Parkinson-White syndrome might be due to the existence of Mahaim fibres, and this has indeed been established by Lev et al. (1966). These workers had carefully followed up a patient who presented with the Wolff-Parkinson-White syndrome which was complicated by right bundle branch block. The patient then went on to develop complete heart block, and died. Pathological examination revealed him to have the bypass fibres of the posterior internodal tract, as well as another tract that ran from the atrial septal muscle into the penetrating portion of the bundle of His. It was considered that this explained the short P-R interval found in the patient. No bundle of Kent was found in the junctional region of the septum or in the right and left parietal walls of the heart, but very copious Mahaim fibres passed from the end of the atrioventricular node and throughout the whole of the bundle of His, into the posterior part of the interventricular septum. This was thought to explain the anomalous ventricular depolarization in this patient; and thus there were two anatomical pathways that bypassed the atrioventricular node and led into the ventricle, causing the appearances of the Wolff-Parkinson-White syndrome.

It has thus been shown that various combinations of anomalous pathways may produce the Wolff-Parkinson-White syndrome, and the presence of single pathways or some combinations may be responsible for atypical variants seen. Review of the possible anatomical pathways and their relationship to the scalar electrocardiogram may offer hypothetical explanations for the bypass in particular cases, which may be summarized as follows:-

1. The classical form of the Wolff-Parkinson-White syndrome consists of shortening of the P-R interval, which does not exceed 0.12 seconds; the QRS interval is widened, measuring 0.12 seconds or longer, and it is deformed by a delta wave. The explanations that might result in this are either:-

(a) the bundle of Kent, with complete bypass of the conducting tissues; or

(b) atrioventricular nodal bypass, e.g. the James fibres, producing the short P-R interval, with subsequent dissemination of the wave of depolarization via Mahaim fibres, producing the delta wave and QRS prolongation, as reported by Lev et al. (1966).

2. Typical[2] Wolff-Parkinson-White syndromes resembling the above features, but not fully meeting the criteria.

(a) normal P-R interval, wide QRS with delta wave; Mahaim fibres only.

(b) short P-R interval, small delta wave, and QRS measuring 0.12 seconds or less;

conduction bypassing the atrioventricular node, the Mahaim fibres producing only partial pre-excitation, as much of the ventricular depolarization must occur via normal pathways.

3. The Lown-Ganong-Levine syndrome, where the P-R interval is short but the QRS complex normal in appearance and duration; an atrioventricular nodal bypass alone would suffice. This could be produced by block in both anterior and middle internodal tracts (Sherf and James, 1969).

These possibilities may be deduced from inspection of Figure 2, which indicates the various possibilities that can be combined, according to Ferrer (1967) and Durrer et al. (1970).

However, the subject is very much in a state of flux, and alternative suggestions exist to explain the pathways present and utilized in the Wolff-Parkinson-White syndrome. On the basis of the results of electrophysiological studies, but without pathological confirmation, Coumel et al. (1971a) have offered the following possible mechanisms, which have been rearranged in table I.

Their reasons for postulating the combination of James and Kent bundles to explain cases of Wolff-Parkinson-White syndrome with a short P-R, delta wave and narrow QRS are discussed in Chapter 6.

On the basis of these classifications, some patients with pre-excitation patterns in the electrocardiogram whose case histories have been analyzed in detail (Section C), fall into the following categories:-

1. Short P-R, delta wave and greatly widened QRS (0.12 seconds or more):- Cases 1, 2, 3, 4, 5 and 6. This is exemplified by figure 3. These could be due to the presence of either

   (a) a bundle of Kent, or

   (b) co-existence of James and Mahaim fibres with <u>conduction in series</u>;

Table I

Conduction pathways according to Coumel et al. (1971a)

Electrocardiographic Appearances	Pathways Postulated
Short P-R, normal QRS	James bundle
Normal P-R, wide QRS + delta wave	Mahaim fibres
Short P-R, wide QRS + delta wave	(a) Bundle of Kent or (b) James bundle + Mahaim fibres
Short P-R, normal QRS + delta wave	James + Kent bundles with conduction in parallel.

2. Short P-R, delta wave and moderately widened QRS (0.08 - 0.11 seconds):- Cases 7, 8, 9, 10 and 11; see figure 4. It seems plausible that the relatively widened QRS is due to the bypass entering the ventricle close to the septum rather than laterally, and anatomical studies might therefore be expected to show the presence of James and Mahaim fibres, though Kent conduction is also possible. The evidence favouring the role of the bundle of Kent in case 7 - and thus possibly in the others - is discussed in Chapter 6; in this patient the criteria of Coumel et al. (1971b) would seem applicable, in that he does not appear to have functioning James fibres.

3. Short P-R, delta wave and narrow QRS:- Case 12 (figure 5). The postulate of James and Kent conduction in parallel to explain this (Coumel et al., 1971a) is attractive.

4. Short P-R, normal QRS: Cases 15, 16 and 18. Their diagnosis is discussed in Chapter 7, on the Lown-Ganong-Levine syndrome.

There are in addition atypical cases who cannot be considered under the terms of this classification, e.g. Cases 13 and 14: see Chapters 11 and 12.

A major difference in approach to conduction in the Wolff-Parkinson-White syndrome was that of Prinzmetal et al. (1952) who postulated that the syndrome was due to accelerated conduction from the sinoatrial, or atrioventricular, nodes, into the ventricles. They propounded their hypothesis of a physiological process that would account for the premature transmission of the excitation wave from the atria to one specific point in the ventricle, producing localized depolarization with its classical appearances, followed by the more general ventricular activity, as seen in this syndrome. It was felt that this accelerated conduction would partly and locally overcome the normal physiological atrioventricular nodal conduction delay. Much of their work was based on experiments on the dog, and the transposition of these studies to the condition obtaining in man with the Wolff-Parkinson-White syndrome does not appear to have been successful. The examples chosen to support this theory, from cases in man, are also dubious. For example, in their cases 7 and 8, where they claim that the P-R interval became shorter after inferior cardiac infarction, it is impossible to confirm this on careful measurement of the published tracings; and in both cases any alteration in the appearance could be explained by technical variations in the tracings. Furthermore, were there an increase in sympathetic tone slight P-R shortening might be produced, without the need to imply that the appearances published provide explanation for the Wolff-Parkinson-White syndrome. One loses more confidence on examining their figure 45, said to show the initiation of paroxysms of ventricular tachycardia by "accelerated conduction beats": the tracing exemplifies idioventricular tachycardia with fusion beats. Finally, this concept as it stands cannot explain the findings seen in patients with the Wolff-Parkinson-White syndrome studied by His bundle electrography, with or without right atrial pacing. Apart from this, the mechanisms for the occurrence of arrhythmias in the Wolff-Parkinson-White and related syndromes cannot be understood using this concept; once the sinoatrial node is no longer the pacemaker, it is difficult to see how the features of pre-excitation could persist, as they do, during atrial fibrillation.

Currently attracting interest as a possible cause of some cases of pre-excitation is the concept of synchronized sinoventricular conduction propounded by Sherf and James (1969). They aver that, if an ectopic supraventricular rhythm were to originate within a tract where fibres bypass a part of the atrioventricular node, each such impulse would reach the lower part of the node before normal stimuli, and would attain its specified destination in the ventricular myocardium and depolarize it prematurely, subsequently to fuse with the later-arriving normally-conducted part of the impulse, producing the typical Wolff-Parkinson-White complex. One would expect an altered P wave morphology when a normal QRS complex is followed by an anomalous one, and this has been noted by Hunter et al. (1940) and by Sanghvi et al. (1959), but I did not find significant changes in the P waves in any of the cases that I have studied, and that are analysed herein. However, as Sherf and James (1969) point out, ectopic foci originating in the posterior internodal tract close to the sino-atrial node will have the same axis as sinus P waves, so this does not contradict their theory, especially as the posterior internodal tract bypasses the atrio-ventricular node and is most often concerned. They recognize most cases of the Wolff-Parkinson-White syndrome as being congenital in origin, but advance as an explanation for its appearance in apparently acquired situations, e.g. rheumatic fever, cardiac infarction and cardiomyopathy, the structural blocking of the anterior and middle internodal tracts. This, they maintain, would force the sinus impulse to descend in the posterior tract, thus bypassing the atrioventricular node; or there might be appropriately located ectopic pacemaking activity that would enable the impulse to enter the posterior internodal tract.

Even if a rare mechanism, this longitudinal dissociation of atrioventricular conduction appears a plausible explanation for some cases of the Wolff-Parkinson-White syndrome.

It must however be stressed that, even with the use of intracardiac electrography, suggestions of which anomalous pathways are responsible are no more than deductions - however logical these may seem - and that much more work is required in the correlation of electrophysiological behaviour and anatomical findings. That this can, albeit rarely. be of practical importance will be seen when the possibility of surgical treatment for intractable arrhythmias is discussed in Chapter 10.

In those cases in whom anatomical studies have been performed, anomalous tracts have not always been discovered; but the technique required for their demonstration is meticulous and demanding (Hudson, 1963), and has not always been used; thus, in both cases of the Wolff-Parkinson-White syndrome examined at autopsy by James, the lateral atrioventricular ring area had not been studied for possible Kent bundles, a third case at present being under detailed scrutiny (T.N. James, personal communication). It is only in those cases where an anomalous pathway is clearly absent that other explanations need be sought. These have, as indicated, been many and varied. Hunter et al. (1940) suggested a double rhythm by two interfering pacemakers, one near the sinus and the other in one bundle branch; but this approach was based on the misapprehension that the wide QRS represented bundle branch block. Then there is the theory that the Wolff-Parkinson-White syndrome is due to the presence of an ectopic focus: in the high posterior septal mass or the right septal mass or free right ventricular wall (Sodi-Pollares et al., 1963). That, in dogs, local stimulation in those areas produces corresponding appearances (Sodi-Pallares, 1957) does not appear to be a firm basis for transposing these findings to the explanation of the Wolff-Parkinson-White syndrome as seen in man. Precise demonstration of this is impossible using present techniques, but some difficult cases might be explained on this basis. The coexistence of intranodal and extranodal pathways has been postulated on the electrocardiographic appearances seen by H.D.

Friedberg and L.Schamroth (1972, in preparation). They recorded electrocardiograms from a 62-year-old man with hypertensive heart disease who was receiving digitalis. These showed intermittent Wolff-Parkinson-White conduction. During the normal-looking complexes, the P-R interval was prolonged, indicating first degree anterograde atrioventricular block. Such beats were followed by atrial echo beats, and runs of reciprocating tachycardia. During the tachycardia, the anterograde conduction times were alternately long and short and they postulate the presence of three atrioventricular pathways to explain this arrhythmia: two in the atrioventricular node, and one outside it.

Indeed, more than one anatomical bypass can exist, and it may be difficult to decide which was responsible for the electrocardiographic appearances. Here mention must be made of a case reported by Lev et al. (1955). Their patient suffered from the Wolff-Parkinson-White syndrome (type B - see Chapter 4), without right bundle branch block, but with the occurrence of paroxysmal atrial tachycardia. At autopsy they noticed the presence of two bypasses, one being a right-sided atrioventricular muscular communication, the bundle of Kent, and the other being communications between the right bundle branch and the right ventricle. They postulated that either pathway could be the cause of pre-excitation in their case; and it is plausible that the emphasis on the function of each pathway may have varied from time to time during life. It therefore does not seem unreasonable that under certain circumstances an anatomical atrioventricular bypass could be responsible for the appearances of the Wolff-Parkinson-White syndrome, and at other times the appearances could be due to longitudinal tract dissociation. Another example of two anomalous pathways operating in the same patient, but not in series, is of course, the parallel functioning of James and Kent fibres postulated by Coumel et al. (1971a) as the explanation for the Wolff-Parkinson-White syndrome with narrow QRS complexes.

The final clinical proof that multiple extranodal pathways may occur in the same patient has now been provided by Ramachandran (1972), whose patient showed (anterograde) type A anomalous conduction during paroxysmal tachycardia, as well as variation from type

A to type B conduction during sinus rhythm. Alternation between types A and B was previously recognized by Scherf and Cohen (1964), but not in association with paroxysmal tachycardia.

A realistic approach to the problem of cardiac pre-excitation at present therefore demands an open mind on the question of atrioventricular nodal bypasses and their importance. Where these occur - as they seem to do in the majority of cases - it is reasonable, should the circumstances fit, to ascribe to them the properties responsible for the production of appearances of the syndrome. In their absence, but only if confirmed by careful anatomical dissection of the heart, longitudinal dissociation may explain at least some cases. The occurrence of both mechanisms should not be excluded when attempting to explain features of the Wolff-Parkinson-White syndrome in appropriate cases. However, present evidence overwhelmingly supports the importance of extranodal anaomalous pathways.

Notes

1. The edge of the wave is perpendicular to the long axis of the atrioventricular node, but the wave travels down parallel to it.
2. Typical in that they present with the main features and belong to the disorder called by the proper name, albeit with atypical features. The term "atypical" has been reserved for presentations like those of Cases 13 and 14.

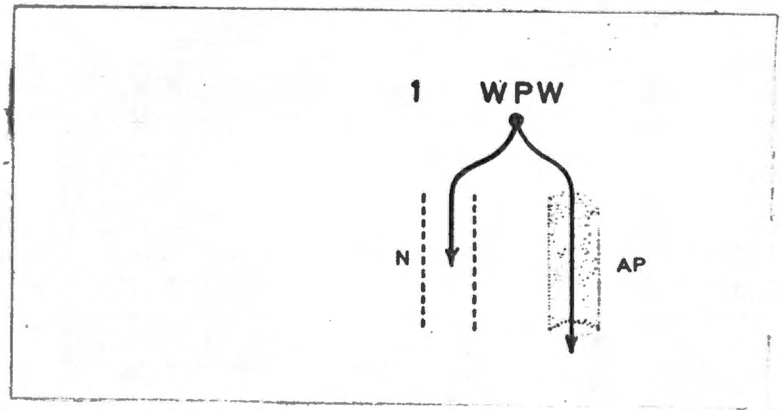
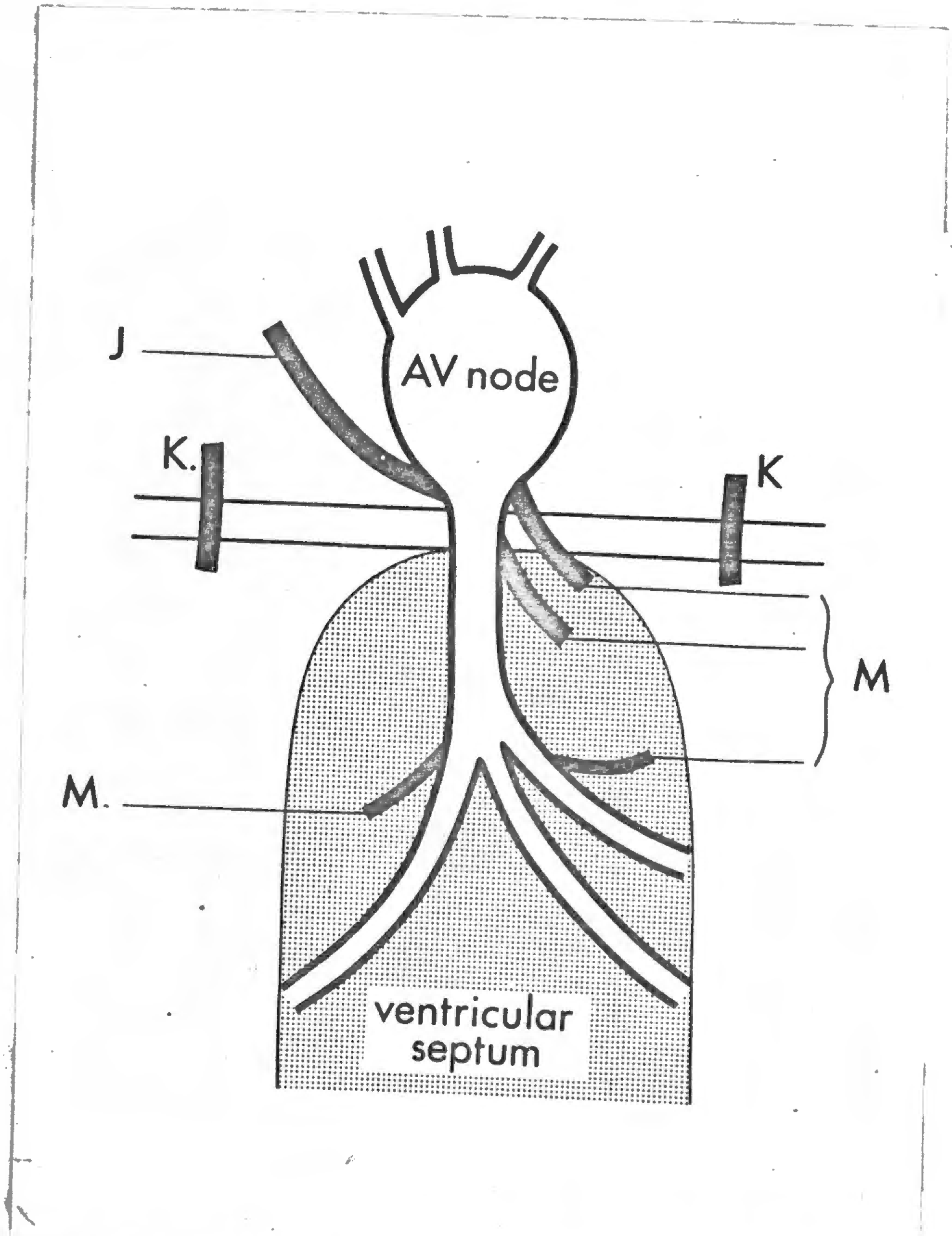


Figure 1 Diagram showing conduction pathways in Wolff-Parkinson-White syndrome.



.Figure 2 Diagram showing normal and anomalous conduction pathways (J = James's fibres; K = bundles of Kent; M = Mahaim tracts). Reproduced from Durrer et al., 1970.

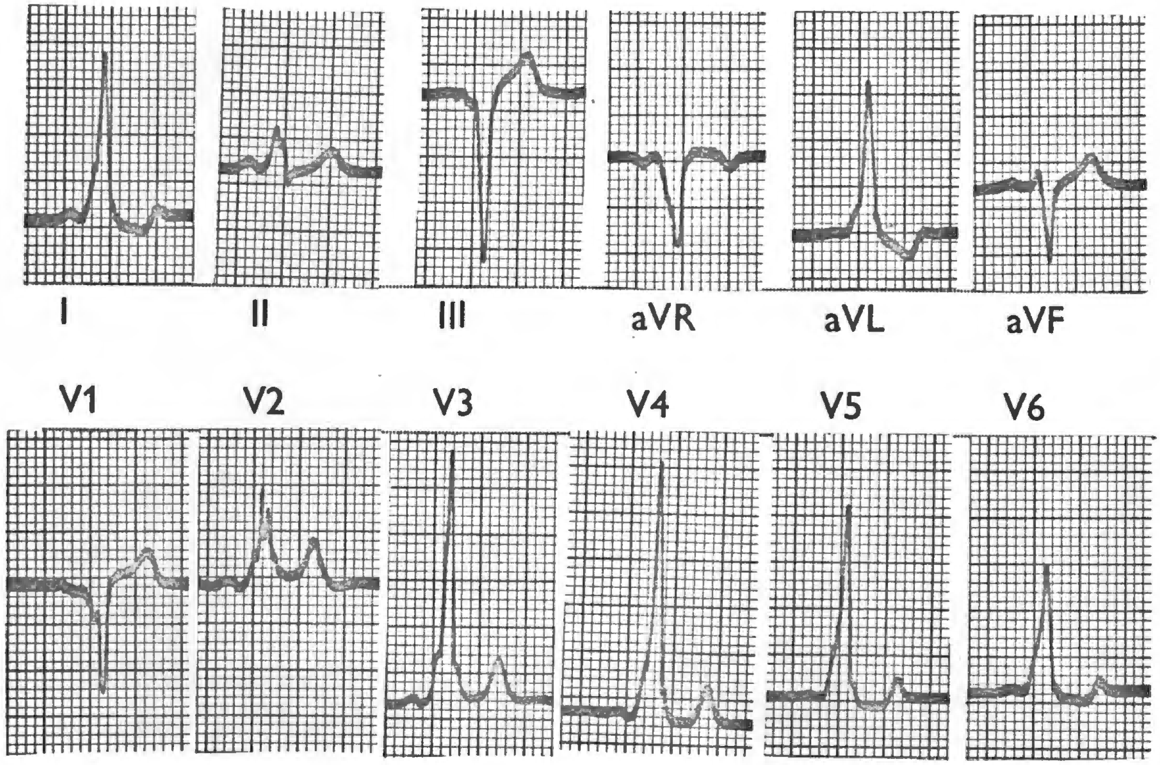


Figure 3 (Case 6) Electrocardiogram, showing Wolff-Parkinson-White syndrome with marked widening of the QRS.

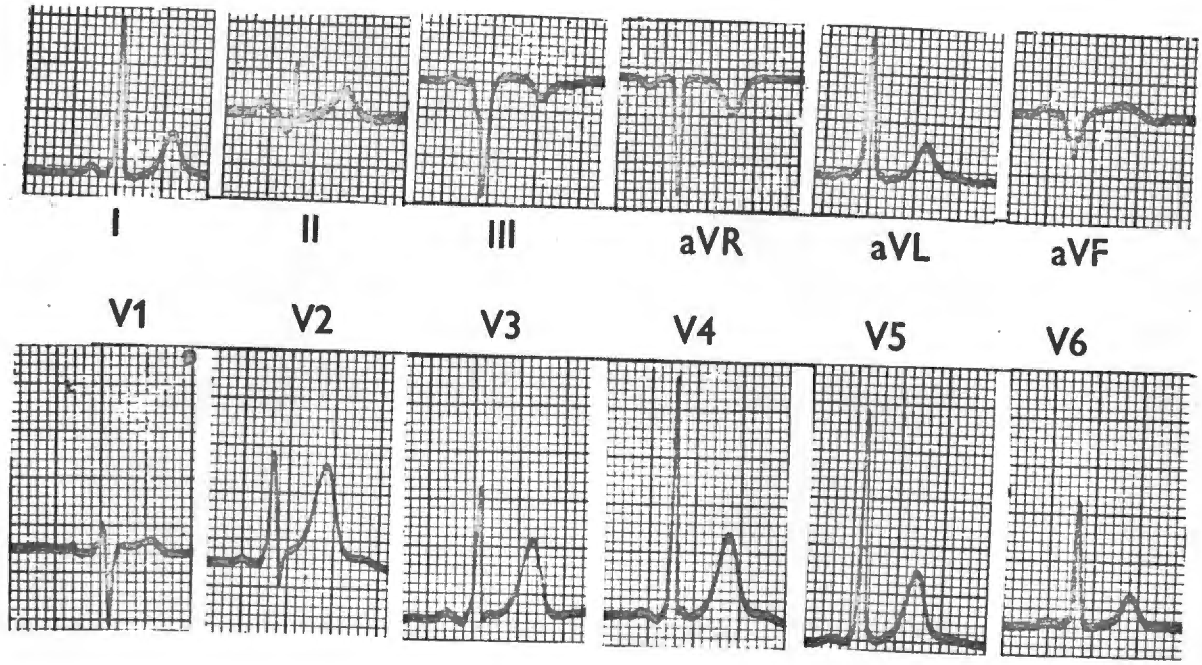


Figure 4 (Case 9) Electrocardiogram showing Wolff-Parkinson-White syndrome with slightly wide QRS.

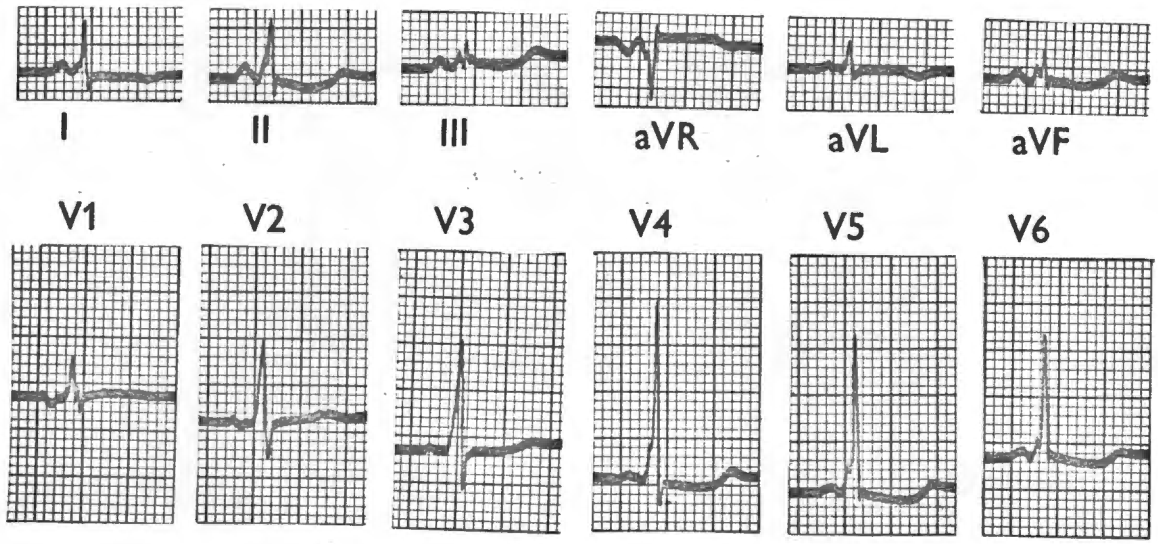


Figure 5 (Case 12) Electrocardiogram showing Wolff-Parkinson-White syndrome type A, with narrow QRS complexes.

CHAPTER 3

The Variability of Pre-Excitation

As the characteristic appearances of the QRS complex in the Wolff-Parkinson-White syndrome is formed by fusion between part of the impulse conducted down the normal pathways with that part that is conducted anomalously, alterations in the degree of utilization of either pathway will consequently lead to greater or lesser emphasis on the particular expression seen. Thus at one time the electrocardiogram may indicate dominance of normal conduction, and at another show total conduction by the anomalous route. A complete range of expression may thus be encountered, different patients revealing their own patterns of behaviour.

That variation in the electrocardiographic appearances is a frequent feature of the Wolff-Parkinson-White syndrome has been recognized from the earliest reports of the condition including those in which it had not yet been defined (Wilson, 1915; Wedd, 1921; Hamburger, 1929; Wolff et al., 1930). Alteration from an anomalous to a normal pattern may be complete ("genuine normalization") or partial ("pseudo-normalization") (Ohnell, 1944), and may occur spontaneously or or after physiological or pharmacological manoeuvres in 24-44% of cases, according to Öhnell (1944) and Averill et al. (1960).

Spontaneous alteration between normal and Wolff-Parkinson-White conduction was the usual finding in Case 1, and is shown in Figure 6. In the first and third complex in each lead, the P-R interval is 0.20 seconds and the QRS is 0.08 seconds. The T waves are inverted in leads III and aVF, but the complexes are all otherwise normal. The second and fourth complex in each lead shows a P-R of 0.10 seconds and a QRS of 0.16 seconds. The upstroke of the R wave is slurred in leads I, II, aVL and V3-6, and the delta waves are most easily visible in V3; there are deep S waves in V1.

An example of more sustained albeit transient spontaneous normalization can be seen in Case 5, where Figure 7 is one of only two (of more than 30 tracings) to show normal conduction. The heart rate was 55 beats a minute, and the P-R interval 0.16 seconds; QRS 0.08 seconds, with slight ST sagging in leads I, aVL and V5 and V6, probably due to digitalis effect. The usual pattern of pre-excitation is shown in Figure 8. The heart rate was 60 beats per minute. The P-R interval was 0.08 seconds (see V6) and the QRS complexes 0.14 seconds. There is a small Q wave in lead 1 and a broad deep Q in aVL. Tall R waves, their initial portions slurred by delta waves, are seen in all the precordial leads as well as lead II, III and aVF; the delta waves are best seen in the left precordial leads. The ST segments are depressed in the precordial leads as well as II, III and aVF.

Partial normalization occurred spontaneously in Case 7. Figure 9 shows his usual conduction pattern. It was recorded during sinus rhythm, and the heart rate was 64 beats a minute. The P-R interval was 0.10 seconds and the QRS 0.10 seconds, ST depression is evident in leads I, aVL and V4 and V5. The upstroke of the R wave is deformed by a delta wave in leads I, aVL and V1-6, and R is the dominant wave in V1. There appear to be deep QS waves in leads III and aVF, with their origins deformed by negative delta waves.

On one other occasion, an electrocardiogram showed features seen in Figure 10. The P-R interval was 0.14 seconds, and the QRS complex was 0.10 seconds. The "Q" waves are less well defined in leads III and aVF, and the delta waves are less prominent, albeit still clearly visible, in leads V2-4. There now however appear to be pathological Q waves in V6 though the situation is less clear in leads II and V5, where a small upstroke immediately follows a small negative wave. These appearances of "pseudo-normalization" incidentally uncover evidence suggestive of otherwise-hidden cardiac infarction (see Chapter 5).

An interesting illustration of "voluntary" alteration in the degree of pre-excitation is seen in Case 2. Figure 11 shows Wolff-Parkinson-White conduction; in Figure 12 there is normal conduction. Figure 11 shows complexes seen when the heart rate averaged 60 beats a minute. The P-R interval is uniformly short, 0.08 seconds, this being most clearly evident in those leads where QRS complexes are most abnormal, including leads I, V5 and V6. The QRS complexes most obviously widened (to 0.12 seconds) in leads showing prominent delta waves; I, III, aVL, aVF, V1, V5 and V6. In leads I, aVL and V3-6, positive delta waves are clearly seen; in leads III, aVF and V1, negative delta waves are equally visible.

In leads III, aVR and V2 and V3, the delta waves are not so clearly visible and the abnormality is not immediately recognizable in them. Inverted T waves are present in leads I, aVL, V5 and V6.

Complexes extracted from the same tracing, that tended to occur when the heart rate averaged 80 beats a minute, are shown in Figure 12. Here the P-R interval is 0.16 seconds, and the QRS 0.08 seconds. T wave inversion is evident in leads II, III, aVF and V6. Normal Q waves can be seen in V5 and V6 as well as I, II, III, aVL and aVF. The upstroke of S in V1 is somewhat slurred.

In this patient, physiological procedures that decreased vagal tone and increased the heart rate produced normalization; those that increased vagal tone and slowed the heart rate brought out the pre-excitation.

His ability to vary the degree of pre-excitation almost at will is shown in Figure 13. The upper strip shows an initial heart rate of 55 beats a minute. The patient then inhaled sharply just prior to the start of the second complex, and the heart rate speeded up to reach 80 beats a minute. Decreasing degrees of pre-excitation can be seen in the third and fourth complexes, which show narrower and shorter QRS complexes, and the fifth complex looks normalized; the sixth, seventh and eighth are undoubtedly so.

In the lower strip, a normal conduction pattern can be seen at a heart rate of 80 beats a minute; at the time of the third complex on this strip, the patient started the Valsalva manœuvre, and the heart rate slowed abruptly to 62 beats a minute, with a sharp transition to the Wolff-Parkinson-White pattern with the sixth beat.

This patient was able to arrange variations of conduction almost at will, with a lag of no more than 3-5 beats. However, whichever rhythm was achieved was unstable and was likely to alter abruptly to the other, sometimes with long periods of alternation of normalized complexes and aberrant conduction. On some occasions there was the abruptness of the transition as seen in Figure 13, (lower strip) and on other occasions this was gradual (upper strip).

Conversion to normal conduction may not be complete - "pseudo-normalization" - and may in addition wax and wane, whether spontaneously or after a manoeuvre like exercise, as is well demonstrated by Case 7. Vigorous exercise in this patient produced a partial and varying degree of normalization, as shown in Figure 14. Throughout this tracing the PJ interval, from the beginning of the P wave to the commencement of the ST segment, was consistent at 0.12 sec., irrespective of changes in the P-R interval and QRS complexes. Almost complete normalization is seen in the first, fourth and seventh complexes, with intermediate degrees of P-R shortening and reciprocal QRS widening in the other complexes. The relatively normal complexes demonstrate the presence of S waves, less marked delta waves, and upright T waves. These changes are also seen in Figure 13 (upper strip). The variation from relatively normal conduction to intermittent Wolff-Parkinson-White pattern has been called the "concertina effect" by Öhnell (1944), who also labelled the almost complete normalization of conduction as "concealed pre-excitation". But the degree of normalization that occurs may vary and take place spontaneously, as is shown in Figure 15. The first, second, fourth and sixth complexes show the pre-excitation patterns.

The P-P intervals between the first and second and the second and third complexes are equal, being 0.96 seconds; and the PJ interval in the first four complexes is 0.24 seconds. Thus the third complex is not an extrasystole but a sinus impulse showing normalization of conduction; it was seen in this lead only, in this particular tracing, and analysis suggests right bundle branch block; but this was not seen in any other tracing taken in this patient, whether during normalization or pre-excitation. The fifth complex is not preceded by a P wave, but is followed by a P' with a R-P' interval of 0.12 seconds, the inverted P' being clearly seen at commencement of the ST segment. This then is a ventricular extrasystole with retrograde atrial conduction.

A most important mechanism of normalization is abolition or reduction of vagal activity; recognition of the importance of the vagus nerve goes back to the observations of Wilson (1915), in whose patient the administration of atropine led to normalization of the QRS complexes. This is a well-established feature of the syndrome, and has been studied by many, including

Duthie (1946), Öhnell (1944) and Averill et al. (1960). Other factors that increase the heart rate have a similar action, e.g. exercise, amyl nitrite, or breath-holding, and responses to these procedures were identified in several cases, albeit not always positively.

In Case 4, an electrocardiogram (Figure 16a) showed the features of the Wolff-Parkinson-White syndrome type A, with a P-R interval of 0.08 seconds, and a QRS interval of 0.14 seconds. There were tall R waves in all precordial leads and positive delta waves could be seen in leads I, II, aVL and V1-6. After exercise there was a slight decrease in the degree of pre-excitation, the P-R interval having lengthened to 0.12 seconds, and the QRS having narrowed to 0.08 seconds (Figure 16b). These changes, and a rightward shift of the mean frontal plane axis of QRS, were most evident in the limb leads and in V1; the delta waves were less marked, and the T wave was less inverted in lead I and not inverted in V1; but by the time V2 was recorded, there had been a return to the more complete pattern of pre-excitation seen in Figure 16a. A greater, but nevertheless still incomplete, degree of normalization can be seen in Figure 16c, recorded in each case during held inspiration. Again, the mean QRS axis has shifted slightly more to the right, P-R measures 0.12 seconds in the limb leads, and the QRS is narrower; more definite S waves are visible in V1-3. A greater, but still incomplete, degree of normalization can be seen after the intravenous administration of atropine, 0.6 mgm (Figure 16d): the P-R appears to be 0.14 seconds in lead III, but reference to leads in which positive delta waves can be seen show that the degree of lengthening is not as great as might be inferred. A more complete degree of normalization of the precordial lead pattern can be seen, but slurring of the upstroke of the R waves can still be seen in leads I, aVL and V3-5 (in panels c and d, V6 was not available).

The gradual alteration from the pattern of preexcitation to a greater degree of normalization can be seen in Figure 17; the arrow indicates the point at which normalization started becoming obvious, which was 45 seconds after the administration of the atropine. This produced an increase in the heart rate from 64 beats a minute prior to the atropine to 104 beats a minute, one minute thereafter.

Case 10, who had the Wolff-Parkinson-White syndrome with a relatively narrow QRS (0.11 seconds) and a P-R interval of 0.10 seconds (Figure 18a), showed complete normalization with both held inspiration (Figure 18b) and after intravenous atropine (Figure 18c), the P-R interval lengthening to 0.20 seconds, and the QRS narrowing to 0.06 seconds; the T waves became inverted in leads II, III and aVF, and the delta waves disappeared. The prompt effect of brisk inspiration is shown in Figure 19: but after two normalized beats, pre-excitation returns. In this patient, the atropine led to normalization through a phase of alternating Wolff-Parkinson-White and normal conduction (Figure 20); the first normal beat appears 25 seconds after the injection.

Such measures sometimes completely fail to produce normalization, even though tachycardia is induced, e.g. by atropine, as in Case 12 (Figure 21), as well as in Cases 1, 5, 6 and 7. In Case 12, supraventricular extrasystoles were associated with normalization (Figure 22, first and last QRS complexes): these presumably found the bypass - but not the atrioventricular node - refractory, by virtue of the time of their occurrence; note the loss of the delta waves. If there are preceding P waves, they cannot be discerned within the preceding T waves. This patient's electrocardiogram during normal sinus rhythm appears in Chapter 2 (Figure 5) when the heart rate was 70 beats per minute. The P-R interval is 0.10 seconds, and the QRS complex measures 0.08 seconds. Tall R waves are present in all chest leads, and delta waves are most clearly visible in leads II, aVF and V4-6. The ST segments are slightly depressed in leads I, II, III, aVF and V4-6, with clearly inverted T waves in I and aVL.

The most complete expression of Wolff-Parkinson-White conduction is seen in atrial fibrillation, when all the impulses may proceed down the bypass, and none down the atrioventricular node and bundle of His and the QRS complex seen on the electrocardiogram is made up of the delta wave alone (Schamroth, 1971a; see also Chapter 8). Under these circumstances, the QRS complex is more bizarre than that occurring during sinus rhythm and different from the normalized QRS occurring during paroxysmal supraventricular tachycardia.

On the other hand, in Case 14, it will be postulated that the complexes reflect occult Wolff-Parkinson-White syndrome, in which all the anterograde conduction occurs down the atrioventricular node and bundle of His during sinus rhythm. If, however, atrial fibrillation is induced, the concomitant physiological atrioventricular block may permit more of the impulse to be conducted down the bypass: see Chapter 11.

No attempt has been made here to assess the influence of digitalis, quinidine or other anti-arrhythmic agents on the appearances of the Wolff-Parkinson-White syndrome during sinus rhythm. It appears that digitalis has a greater effect on the atrioventricular node than on the anomalous pathway (Scherf and Schonbrunner, 1935; Wolff and White, 1948) thus tending to increase conduction down the latter. Quinidine and procainamide, on the other hand, tend to block the anomalous pathway to a greater extent than the atrioventricular node, and tend to produce normalization (Roberts and Abramson, 1936).

What might determine whether or not the atrioventricular node or the anomalous pathway is used for anterograde conduction at any particular time? Why and how do the procedures considered above produce their effects? Why is the Wolff-Parkinson-White pattern so often unstable and in some patients spontaneously or by various mechanisms normalized? We do not have a full picture of all the factors, but some recent developments shed new light on these questions. Basic electrophysiological studies have again helped in the understanding of what is seen on the electrocardiogram.

Mendez et al. (1970) have introduced the concept of a mismatch impedance to account for the failure of impulses to be propagated across the junction between the Purkinje fibres and cardiac muscle cells. If it has an adequate cable capacity, the filament conducting the current will transmit it. On the other hand, if the cable capacity is small, especially in relation to a relatively large muscle mass which it enters and has to activate, transmission may not occur.

As Schamroth (1971a) has pointed out, the atrioventricular nodal pathways are not subject to this sort of difficulty because they have a large cable capacity and are directly connected with the specialized conducting system. An anomalous pathway, on the other hand, may be complicated by this form of mismatch impedance, and not transmit impulses which enter it, whereas the conventional pathways are able to do so. Conduction in the reverse direction, i.e. retrogradely up the anomalous pathway, is easy to achieve, because conduction enters the pathways <u>from</u> a large muscle mass.

If there is much mismatch impedance between the anomalous pathway and its ventricular destination, conduction down the normal atrioventricular nodal pathways will be favoured. If on the other hand this mismatch impedance is dissipated, the anomalous pathway may be utilized successfully, and be able to initiate depolarization of the area of ventricle into which it is inserted. At present insufficient is known of the factors that may alter this situation. The possible sites of action are:-

(a) <u>The atrioventricular node</u>

If conduction in this structure is blocked or delayed, activation via an anomalous pathway is to be anticipated. Vagotonic manoeuvres have this tendency, and this might well in part explain the fact that digitalis tends to favour conduction down the anomalous pathway. The physiological second-degree atrioventricular nodal block produced by rapid atrial pacing could thus account for the increasing degrees of pre-excitation produced by this technique (see Chapter 6). The varying degrees of atrioventricular nodal block during atrial fibrillation could also in this way explain the tendency for there to be greater or even total anomalous conduction during atrial fibrillation.

The importance of disease of the atrioventricular conduction tissue in possibly determining utilization of an anomalous pathway is supported by the high incidence of pathological changes in the conduction system seen in cases of the Wolff-Parkinson-White syndrome examined at autopsy (De Mesquita, 1955). An alternative explanation would be that of Sherf and James (1969), that the diseased conduction tissue leads to accelerated conduction within neighbouring portions that are unaffected.

(b) The anomalous pathway

There may be direct effects on a bypass tract. This has been demonstrated, and the concept of mismatch impedance and its existence and dissipation in relation to the Wolff-Parkinson-White syndrome has been strengthened, by recent studies by De la Fuente et al. (1971). These workers dissected isolated blocks of atrial tissue from dogs, in order to provide a narrow isthmus connecting two broader areas. They were easily able to demonstrate unidirectional block at the junctions of the narrow band with the larger areas. Acetylcholine restored 1:1 propagation in blocked preparations. Thus, some vagotonic measures may encourage anomalous conduction by virtue of a direct effect on the bypass tract, as well as through a blocking effect on atrioventricular nodal transmission.

(c) The ventricle

Here little is known of factors that may increase inpedance: speculatively, if this did occur, it is a possible means of inhibition of pre-excitation. While the precise way in which quinidine and procainamide tend to favour normalization is unknown, one may postulate that their action is on the ventricular muscle, and that they influence it in such a way that it requires a larger depolarizing current than is available to traverse the bypass and produce a response in the pre-excitation area.

It is also plausible that some factors may decrease the amount of current required to initiate localized ventricular depolarization via an anomalous pathway. That this may be concerned in myocarditis and cardiomyopathy is considered in Chapter 12; this may also obtain in myocardial infarction. Thus what may appear to be an acquired Wolff-Parkinson-White syndrome due to the above disorders may really be the bringing to light of a hitherto entirely latent bypass.

Moulopoulos et al. (1971) have proposed an explanation for the variability of the Wolff-Parkinson-White syndrome in relation to the heart rate, on the basis of five cases they have studied. They suggest that the factor producing cardiac acceleration may affect the sinoatrial and atrioventricular node and the anomalous pathway to different degrees. It may be more to the point to relate the effects seen to the response of the atrioventricular node and the anomalous pathway to the degree of mismatch impedance between the latter and the ventricle. That which tends to block the conduction of impulses down the atrioventricular node will make available a larger current to traverse the anomalous pathway; this will diminish any potential mismatch impedance between the anomalous pathway and the large-volume recipient ventricular mass into which it is inserted. The same factors that tend to cause atrioventricular nodal block might concomitantly enhance conduction down the anomalous tract, as evidenced by the response to cholinergic stimulation (De la Fuente et al., 1971). This will bring out pre-excitation; whether the converse also applies remains to be seen. Indeed it does not appear to be the heart rate that is the determining factor leading to normalization, but rather the direct effects of the physiological or pharmacological procedures on the atrioventricular node or the bypass, or on both. This is suggested by work mentioned by A.N. Damato at a symposium on arrhythmias in Amsterdam in March 1972. When patients with the Wolff-Parkinson-White syndrome had their hearts paced at the rate of 120 beats a minute, anomalous conduction persisted. If, with the heart rate maintained unchanged, isoprenaline or atropine were given, normalization could be achieved, i.e. without an increase in the tachycardia.

The question of normalization has been looked at in a slightly different way by Massumi and Vera (1971) who delineated four sets of circumstances under which this could occur - failure of anomalous conduction at high atrial rates or with very early extrasystoles; phase 4 depolarization of the anomalous pathway, rendering it refractory, after long pauses and in slow rhythms; initiation of the impulse below the origin of the anomalous path; and when conduction velocity was faster in the normal than in the anomalous conduction pathway. Some of these points provide additional understanding of the occurrence of normalization under specific circumstances; their paper provides a useful contribution and some helpful illustrations.

Much remains for us to learn of what determines why normal or anomalous conduction occurs at different times or under certain circumstances in patients with the Wolff-Parkinson-White syndrome, but the above concepts appear to clarify this question.

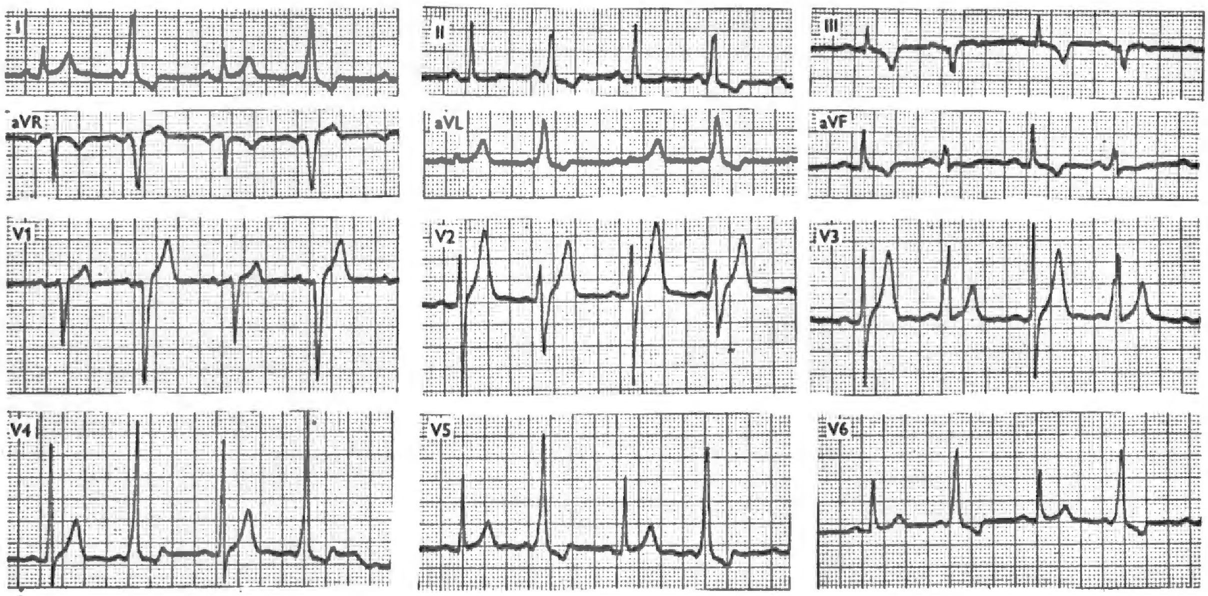


Figure 6 (Case 1) Electrocardiogram, showing sinus rhythm, with normal conduction alternating with Wolff-Parkinson-White conduction.

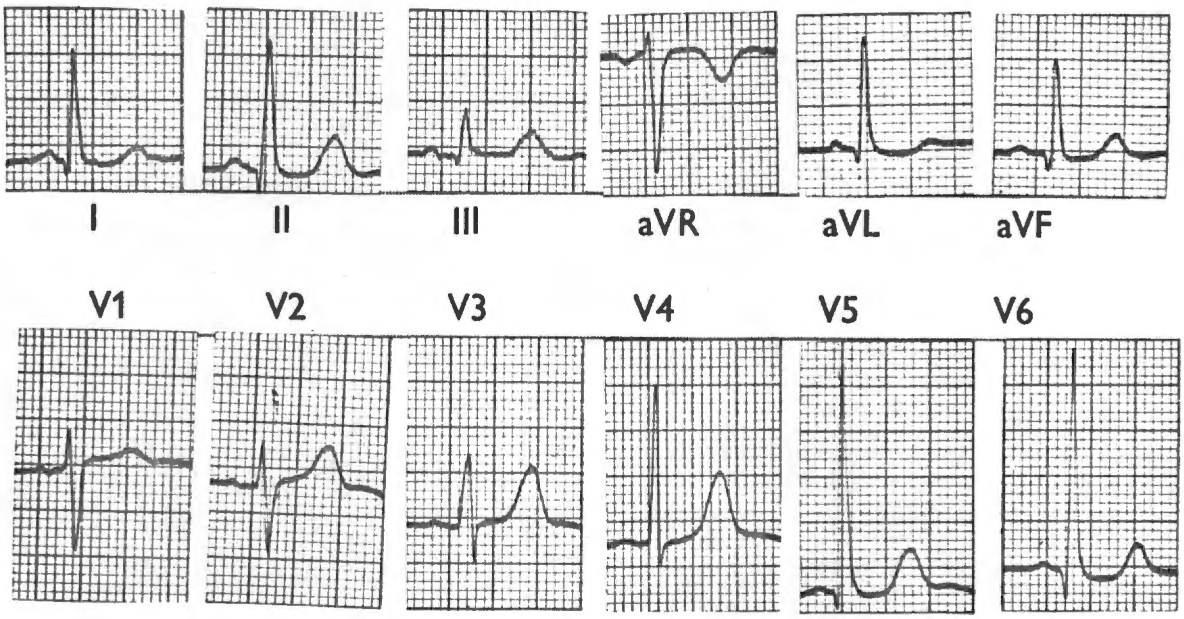


Figure 7 (Case 5) Electrocardiogram showing sinus rhythm and normal conduction.

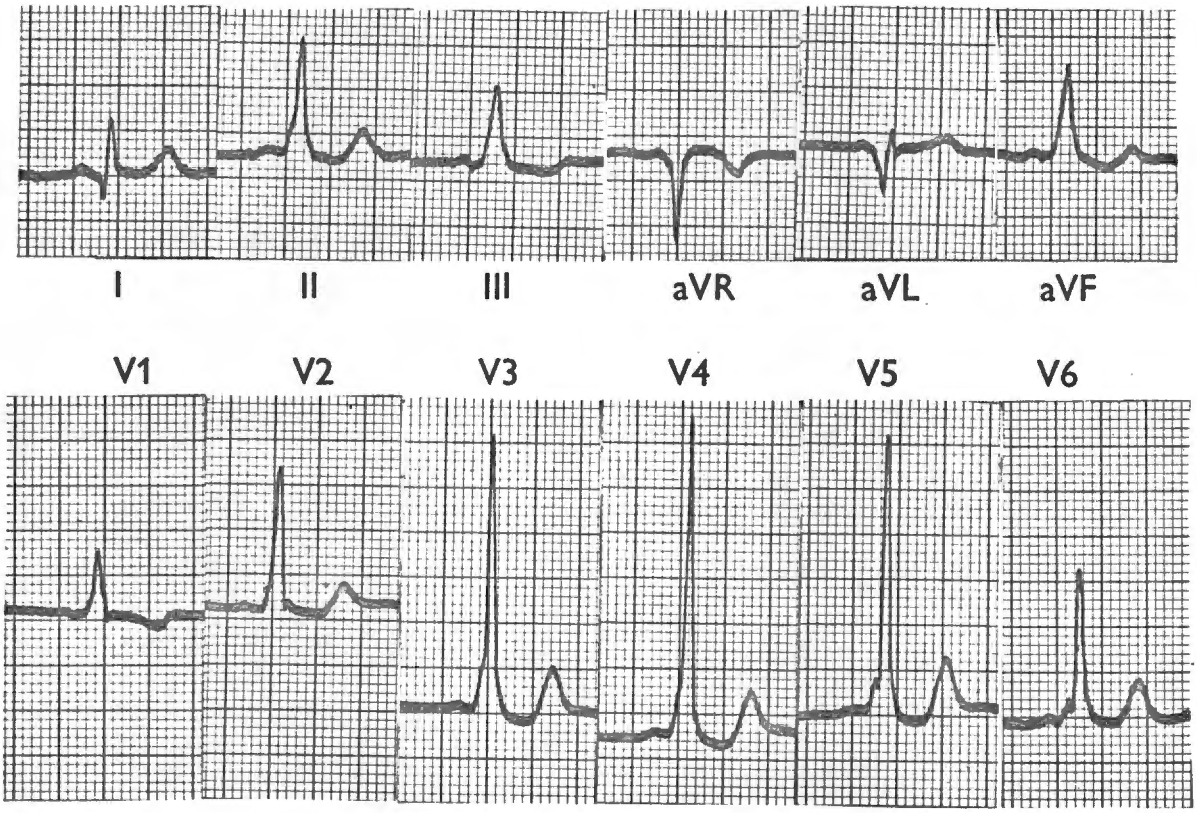


Figure 8 (Case 5) Electrocardiogram showing sinus rhythm and Wolff-Parkinson-White syndrome.

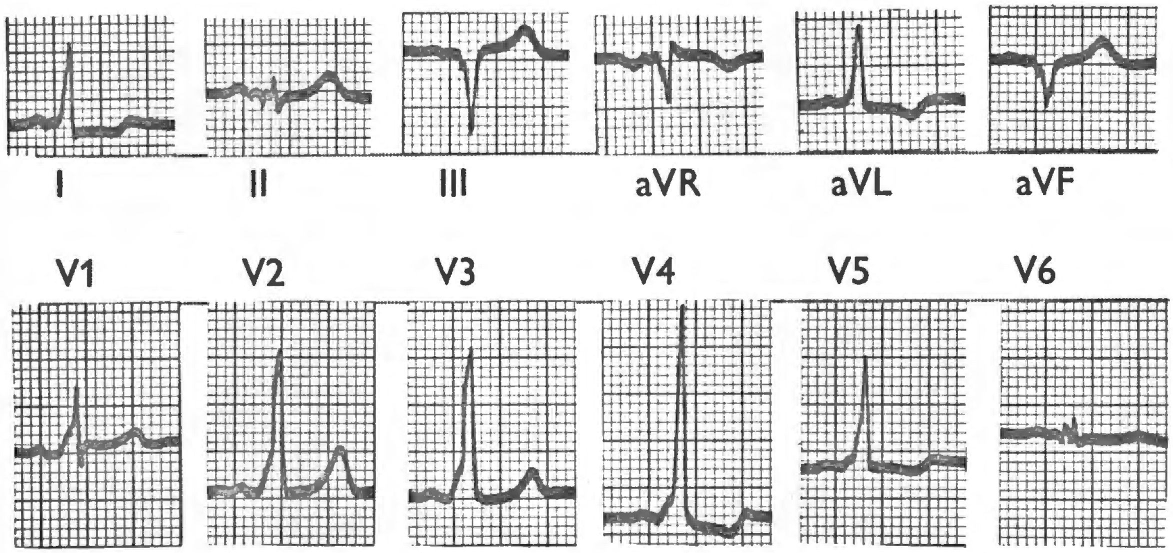


Figure 9 (Case 7) Electrocardiogram showing Wolff-Parkinson-White syndrome.

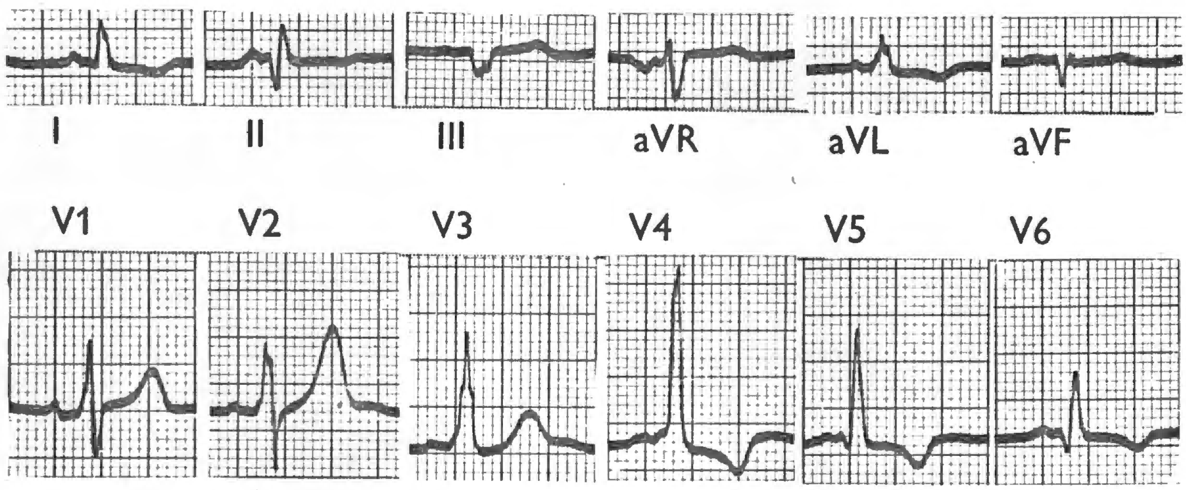


Figure 10 (Case 7) Electrocardiogram showing incomplete picture of pre-excitation.

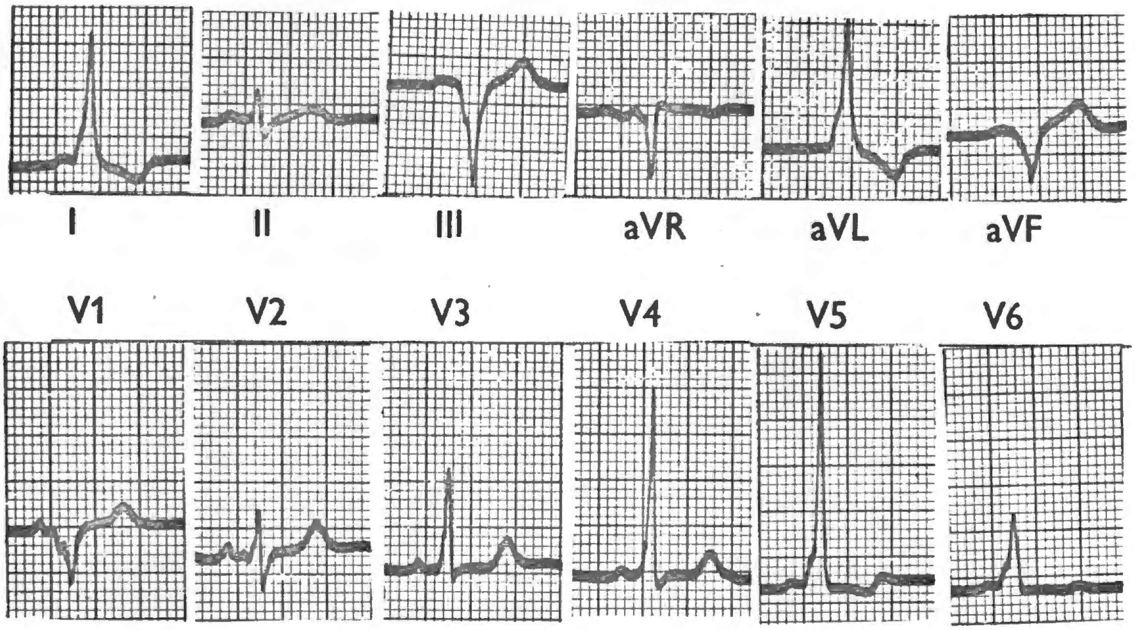


Figure 11 (Case 2) Electrocardiogram showing Wolff-Parkinson-White syndrome.

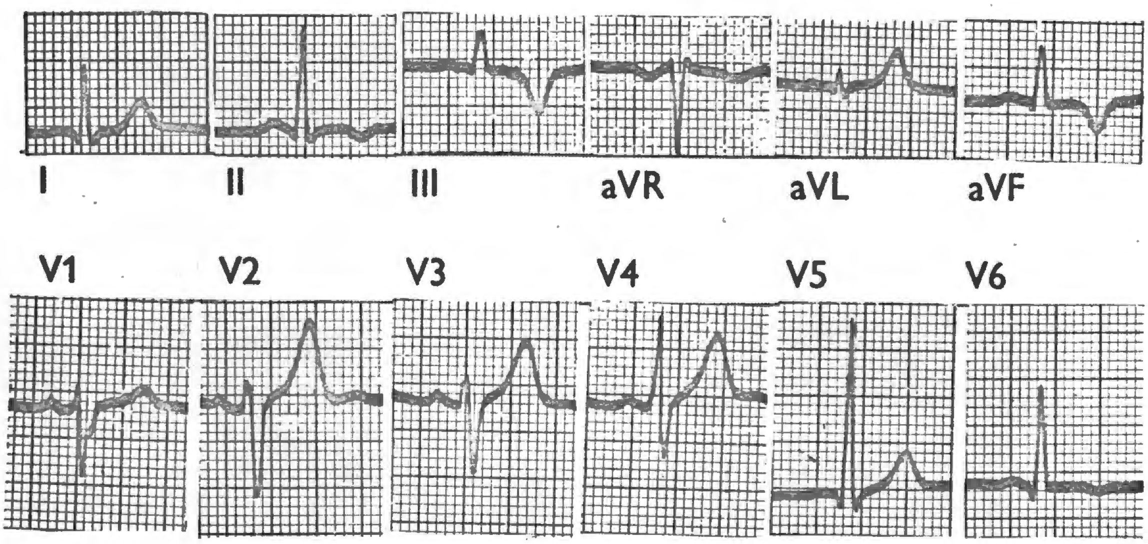


Figure 12 (Case 3) Electrocardiogram, showing normal conduction.

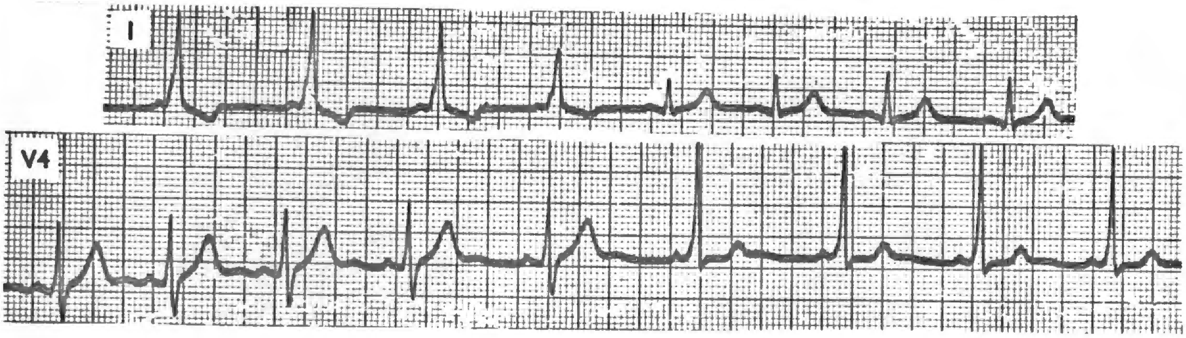


Figure 13 (Case 2) Electrocardiographic strips, showing:-
Lead I: Conversion from Wolff-Parkinson-White to normal conduction with brisk inspiration;
V4: Conversion from normal to Wolff-Parkinson-White conduction with the Valsalva manoeuvre.

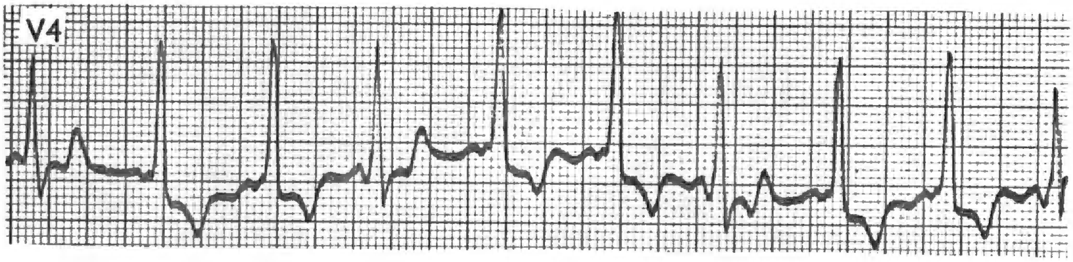


Figure 14 (Case 7) Electrocardiographic strip (V4) after exertion, showing varying degrees of pre-excitation ("concertina effect").

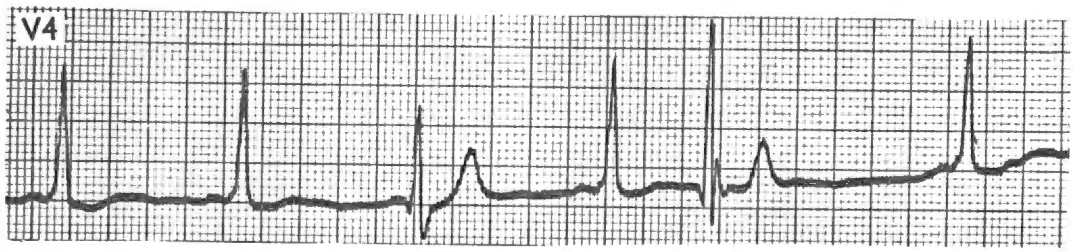


Figure 15 (Case 7) Electrocardiographic strip (lead V4) showing sinus rhythm with diminished pre-excitation in the third complex, and a ventricular extrasystole as the fifth.

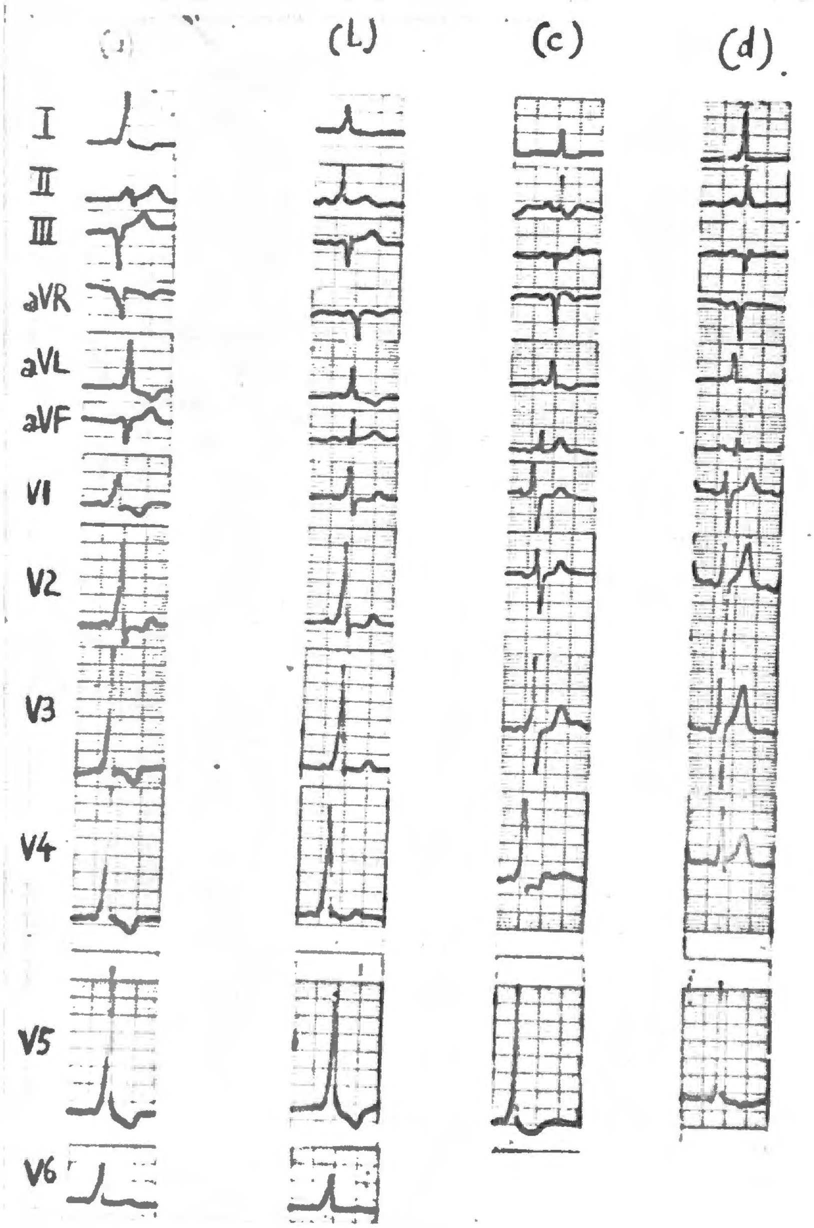


Figure 16 (Case 4) Electrocardiogram,

(a) Wolff-Parkinson-White conduction at rest
(b) after exercise
(c) after inspiration
(d) after atropine

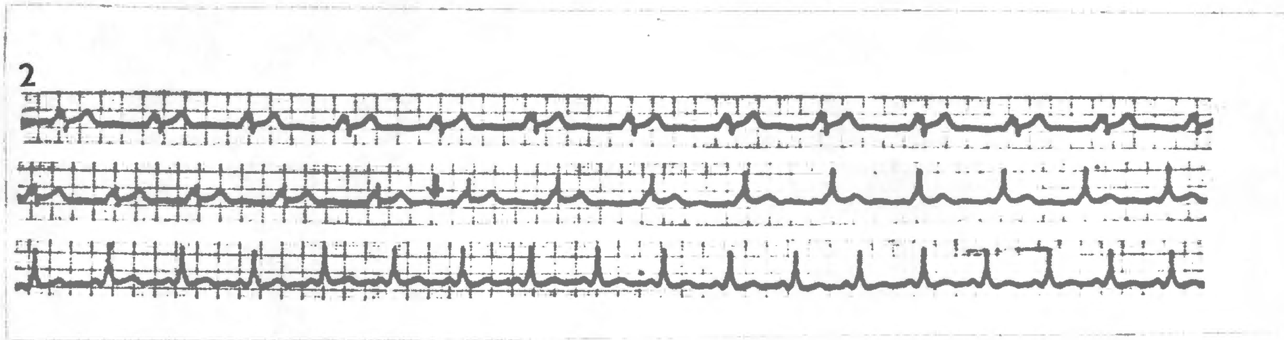


Figure 17 (Case 4) Electrocardiographic strip, showing gradual conversion of Wolff-Parkinson-White to normal conduction after intravenous atropine (arrow = 45 seconds after injection).

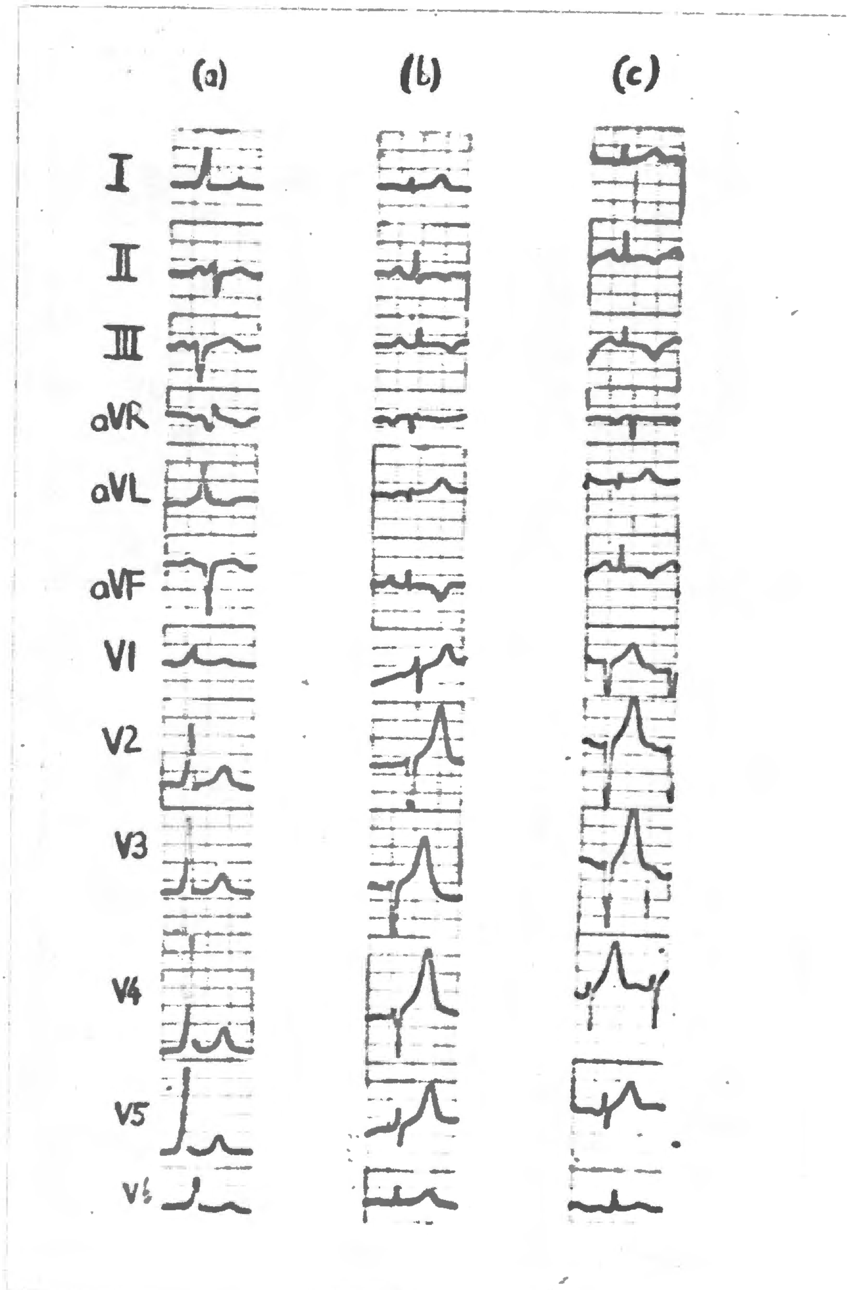


Figure 18 (Case 10) Electrocardiogram,

(a) Wolff-Parkinson-White conduction at rest
(b) after exercise
(c) after atropine

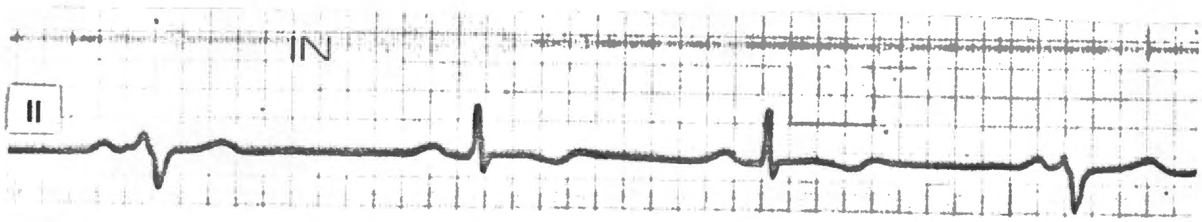


Figure 19 (Case 10) Electrocardiographic strip showing conversion of Wolff-Parkinson-White conduction to normal during deep inspiration; upper strip shows the sound of the inspiration using a phonocardiographic channel.

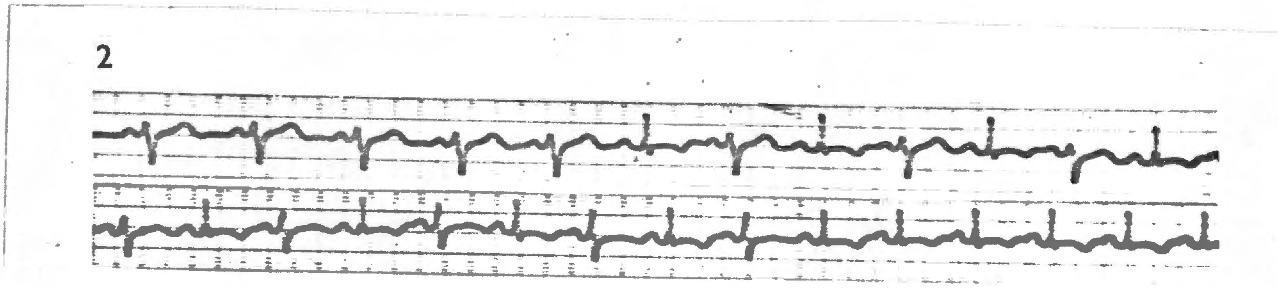


Figure 20 (Case 10) Electrocardiographic strip showing conversion of Wolff-Parkinson-White to normal conduction after intravenous atropine.

Figure 21 (Case 12) Electrocardiographic strips at rest (aVF) and after atropine (lead II).

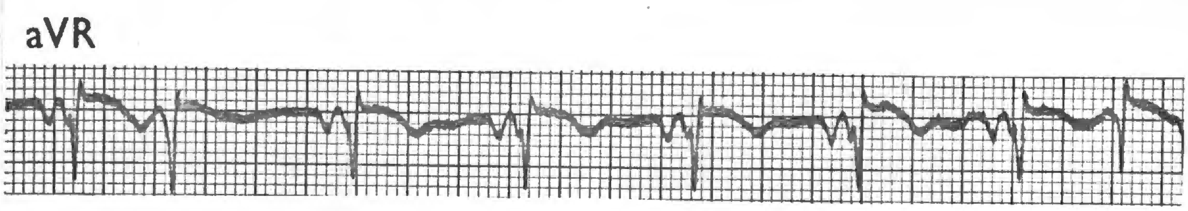


Figure 22 (Case 12) Electrocardiographic strip showing normalization of conduction by supraventricular extrasystoles.

CHAPTER 4

The Location of the Pre-Excitation Areas in the Wolff-Parkinson-White Syndrome

Rosenbaum et al. (1945) were the first workers to assess the Wolff-Parkinson-White syndrome using the unipolar chest leads in a large series. They divided their cases into two groups, depending on the configuration of the QRS complex in the right precordial leads (V1 and V2). Those cases in which the QRS complex was predominantly positive, i.e. in which the R wave was the sole or largest deflection in thôse leads, were labelled type A; examples of this can be seen in Figures 5, 8, 9, 16, 18.

On the other hand, when the QRS complex was predominantly negative in those leads, i.e., where there was a prominent S wave, they labelled the group type B. Examples of this can be seen in Figures 3, 4, 6, 9, 11, 23.

In the other chest leads, irrespective of the classification, predominant R waves with positive delta waves are the rule.

In type B, as defined in this manner, no reference is made to the direction of the delta wave. Holzmann (1962) has classified the Wolff-Parkinson-White syndrome on the basis of the direction of the delta wave, into a sternal positive (with positive delta wave in leads V1 and V2) and a sternal negative type (with negative delta waves in the same leads); he feels that these correspond to types A and B respectively. However, perusal of Figures 4 and 23 shows that it is possible to have a positive delta wave in V1 together with a large S wave in the same lead, so correspondence is not precise. In addition, in not all cases is the delta wave invariably positive and the first visible deflection in the left precordial leads; small q waves can sometimes occur (Figure 10). This almost certainly reflects pseudo-normalization with, in this case, underlying anterolateral cardiac infarction revealed, rather than a negative left precordial delta wave: the latter is something that Wolff (1964) considers to be incompatible with the diagnosis of the Wolff-Parkinson-White syndrome. The significance of the minute Q in Figure 25 is doubtful; it appears to controvert this statement.

According to Scherf and Cohen (1964), type A is much rarer than type B, but according to a personal communication from D. Durrer, this is not the experience of the Amsterdam group. Of the cases discussed in Section C seven were type A, four were type B and Case 9 had a positive delta wave in V1 but meets the criteria for type B (Rosenbaum et al., 1945).

Obviously, classification into types in this way is only of importance if there is significance relating to the underlying mechanism of pre-excitation in the Wolff-Parkinson-White syndrome. Rosenbaum et al. (1945) and Holzmann (1962) also used oesophageal and intra-cavity leads and reached the conclusion that type A conduction was seen when the posterior portion of the left ventricle was first activated, and the ventricular activation followed an inferior direction; type B was observed when the activation was at the anterolateral aspects of the right ventricle, near the atrioventricular border, taking place in a right-to-left and inferor-superior direction.

An important study was that of Giraud et al. (1956), in which they performed intra-cavity electrocardiograms on six patients with the Wolff-Parkinson-White syndrome. They concluded that type A represented early activation of the left ventricle and type B, early activation of the right ventricle. Similar conclusions were drawn by Bilger et al. (1962) and Bilger and So (1963). Scherf and Cohen (1964), on the other hand, consider that the direction of the delta wave in V1 depends on trivial differences of the direction of the delta wave vector, which in most instances is more or less parallel to the frontal plane; they thus questioned whether types A or B could permit the diagnosis of a different location of the pre-excitation area. If however, as they have found, both type A and type B may be found in the same patient at different times, this may represent the presence of more than one anomalous pathway between atria and ventricles, rather than minor changes in the vector within a single bypass.

The existence of these two types of Wolff-Parkinson-White syndrome suggests the presence of two different ventricular pre-excitation sites. As indicated above, it is believed by some that the pre-excitation site is situated in the left ventricle in type A and in the right ventricle in type B. This concept was demonstrated experimentally by Peñaloza et al. (1963) who observed that the type B conduction in the Wolff-Parkinson-White syndrome made normal experimental right bundle branch block (induced during cardiac catheterization by pressure on the right side of the interventricular septum by an electrode catheter); the type A form of conduction, however, had no effect. This suggested that in right bundle branch block with type B Wolff-Parkinson-White syndrome, the ventricular myocardium normally activated by the right bundle branch receives the impulse through the anomalous pathway; the pre-excitation area is therefore located in the right ventricle distal to the blocked right bundle branch.

Schamroth and Krikler (1967a) reported two clinical cases in which the co-existence of right bundle branch with types A and B Wolff-Parkinson-White syndrome, respectively, provided an opportunity to test this hypothesis. Their case 1 (here reported as Case 8) suffered from Ebstein's disease of the tricuspid valve. In her electrocardiogram (Figure 23) the rhythm was regular, but there was a variation with two distinct patterns seen respectively in alternate beats. The first beat in each cycle shows sinus rhythm with normal conduction; the second beat shows sinus rhythm with the pattern of Wolff-

Parkinson-White conduction, type B. The beats with normal conduction show a P-R interval of 0.20 seconds, and a QRS of 0.08 seconds. The mean frontal plane QRS axis is + 105°. Deep S waves are evident in leads I, aVL and V6, with changes in right precordial leads indicative of right bundle branch block, best seen in V3 as rSR's', with T wave inversion in leads II, III, aVF, and V1-5. In the alternate complexes, the P-R interval is 0.10 seconds, and the QRS 0.12 seconds. Deep S waves are evident in leads V1 and V2, and the upstroke of the R wave is deformed by a delta wave in leads I, aVL and V6; slurring of the initial portion of the QS wave is clearly visible in lead III. (In aVR, the anomalous beat is the first in the cycle). In their second case, the electrocardiogram was recorded from a 24-year-old woman who complained of palpitations, and in whom physical examination was essentially negative. It showed type A Wolff-Parkinson-White complexes associated with an underlying right bundle branch block pattern. The classic right bundle branch block pattern was revealed by the widened QRS complex, R' deflections in V1, and delayed and slurred

S waves in leads I, aVL, V5 and V6. The Wolff-Parkinson-White syndrome was diagnosed by the presence of the delta wave and the type A form by the associated ensuing tall R wave in leads V1 and V2; the tall R wave constitutes the initial vector of the QRS complex proper. The P-R interval measured 0.12 seconds.

Two further cases illustrate the coexistence of right bundle branch block and type A Wolff-Parkinson-White conduction. In Case 3 the electrocardiogram (Figure 24) showed sinus rhythm at the rate of 100 beats a minute. The P-R interval was 0.10 seconds and the QRS 0.16 seconds. A small Q wave, being a negative delta wave, is visible in lead I, and there is a QS in aVL. The upstroke of R is clearly slurred by delta waves in all precordial leads as well as leads II, III and aVF. This delta wave is more definitely brought out at a paper speed of 50 mm. a second, as in the bottom panel of Figure 24.

In addition to the features of the Wolff-Parkinson-White syndrome, type A, there are deep S waves in leads 1, and V6, and the R' can be discerned as a double summit in V1. This together with the QRS widening to 0.16 seconds, indicates the presence of right bundle branch block in addition to the Wolff-Parkinson-White type A.

Despite exercise, 0.6 mg. of atropine intravenously, and forced inspiration, the features of the Wolff-Parkinson-White syndrome persisted.

The first tracing in sinus rhythm of Case 11 (Figure 25) was taken immediately after sinus rhythm had been restored, by intravenous verapamil, from paroxysmal supraventricular tachycardia. The heart rate was 100 beats a minute. The P-R interval is 0.08 seconds and the QRS complexes are 0.10 seconds wide. The upstroke of R is deformed in leads II, III, aVF and V1-5 by delta waves, and there is ST depression and/or T wave inversion in leads II, III, aVF and V1-5. The delta wave is not clearly visible in V6, the initial complex there appearing to be a minute Q wave. In addition, the end of the downstroke of the tall R wave in V1 is deformed by a minute upstroke, r', and there are minute S waves in V5 and V6. These features are in keeping with the presence of the Wolff-Parkinson-White syndrome, type A, complicated by right bundle branch block. In those leads where the delta wave is isoelectric, e.g. aVF and V6, the P-R interval appears lengthened to 0.12 seconds as the QRS complexes apparently narrow to 0.05 seconds.

Twenty-four hours later, a tracing showed less evidence of pre-excitation and more of right bundle branch block (Figure 26). The heart rate was 70 beats a minute, and one must assume that there was less pre-excitation with the relative bradycardia, compared to that shown in Figure 25 (100 beats a minute). Delta waves are again clearly visible, this time in leads II, III, aVF and V3-4, being less clear in V5, probably negative in V6, and clearly inverted in leads I and aVL; in aVR, where it is isoelectric, the P-R interval again appears to be 0.12 seconds. An rSr' pattern is visible in leads V1 and V2, and the features are in keeping with the Wolff-Parkinson-White syndrome, type A, with somewhat less pre-excitation, and a greater emphasis on the right bundle branch block. The predominantly downward QRS complex in V1 might suggest that this is a case of the Wolff-Parkinson-White syndrome type B, but reference to Figure 25 shows that this is better diagnosed as type A.

It is quite clear that the pre-excitation from type B Wolff-Parkinson-White syndrome in Case 8 makes the coexisting right bundle branch block pattern normal, whereas the pre-excitation from type A in Cases 3 and 11 (and in Case 2 of Schamroth and Krikler, 1967a) does not. This indicates (1) that the anomalous pathway in type B is situated between the atria and right ventricle, and activates the right ventricle distal to the block and (2) that the anomalous pathway in type A does not reach this region and is therefore situated between the atria and the left ventricle. These conditions are depicted in Figure 27, and are supported by the findings of Richmond and Pordy (1969).

These observations support the experimental work of Gamboa et al. (1962) and Peñaloza et al. (1963) and help to explain other related observations. Thus, Cabrera et al. (1959) observed varying degrees of normalization of the right bundle branch block pattern in a case of Ebstein's anomaly in which type B Wolff-Parkinson-White syndrome was associated with right bundle branch block. The degree of right bundle branch block varied inversely with the degree of pre-excitation: the greater the degree of pre-excitation, the more the normalization of the bundle branch block pattern, and vice versa. Advanced degrees of both patterns were never present simultaneously. This is very similar to the situation in Case 11 (see Figures 25 and 26). Cabrera et al. (1959) also concluded that the pre-excitation area of the Wolff-Parkinson-White type B syndrome is located in the right ventricle. As in Case 3 and 11, in a patient reported by Pick and Fisch (1958) (their case 1), the pattern of right bundle branch block was not made normal by the coexistence of type A Wolff-Parkinson-White syndrome.

Durrer et al. (1970), however, have observed that type B pre-excitation may occur in association with right bundle branch block. Two such cases, i.e., occurring without normalization of the pre-excitation pattern by the right bundle branch block, have been noted; by Robertson et al. (1963) and by Fernandez Caamano et al. (1967). Under these circumstances, it is difficult to maintain that the bypass producing anomalous conduction is a lateral pathway, i.e. the bundle of Kent. It is much more likely that Mahaim fibres originate from the bundle of His, on the right side, and entering the myocardium of the interventricular septum, also on the right side, give rise to the delta wave and the typical changes in the QRS complex, albeit modified by the occurrence of block further down the right bundle branch. Right ventricular pre-excitation failed to abolish right bundle branch block in two patients, but the relevance of their technique to the state of affairs in the Wolff-Parkinson-White syndrome is uncertain. In their artificial model, the pre-excitation was produced proximal to the block so, as they concede, it would not have been expected that the appearances of right bundle branch block would have disappeared. Indeed, according to Gersony and Ekery (1969) right bundle branch block that is not normalized by type B Wolff-Parkinson-White conduction is peripheral rather than central; but as indicated above, it is at least as plausible that the bypass is central (Mahaim tracts) rather than peripheral and lateral (bundle of Kent).

Not only is the question of where the bypass is of considerable academic interest; it may well be crucial to know this when surgical treatment of intractable arrhythmias due to the Wolff-Parkinson-White syndrome is contemplated. Further analysis of this question is thus potentially fruitful.

Further support for the concept that the bypass is right-sided in type B and left-sided in type A Wolff-Parkinson-White syndrome comes from recent studies using right and left heart stimulation in such cases. In a patient with the type B syndrome the pattern of epicardial excitation was explored during cardiac surgery (Durrer and Roos, 1967). This revealed that, during pre-excitation, a portion of the right ventricle, at its lateral border near the atrioventricular sulcus, was activated about 150 milliseconds earlier than could be expected if this region had been activated normally, through the conventional atrioventricular conducting system. It was possible to demonstrate that this area of early depolarization was followed by an epicardial excitatory wave which spread across the ventricular surface; the epicardial surface of the left ventricle was activated normally. These findings have been corroborated by Burchell et al. (1967) and by Cobb et al. (1968), when the early activation areas were divided surgically in order to interrupt the presumed reciprocal pathway responsible for intractable paroxysmal tachycardia. This is considered further in Chapter 10.

The results of the work of Durrer et al. (1970) suggest that Mahaim fibres on the right side of the interventricular septum, if activated early, can produce the appearances of the Wolff-Parkinson-White syndrome type B; whereas if the point of insertion is located near the left side, the complexes will be of type A. An interesting suggestion is that such Mahaim fibres inserted into the middle of the interventricular septum will possibly produce pre-excitation without there being appreciable changes in the QRS complexes of conventional leads because the excitatory front is not directed to either side and thus does not produce a detectable delta wave. However a bypass will still exist even though not easily detected, and that this may explain some cases of paroxysmal supraventricular tachycardia apparently due to a re-entry mechanism.

Studies of cardiac stimulation aimed at producing tachycardias in these patients were also conducted by these workers (Durrer et al., 1967). They found that, in patients with the Wolff-Parkinson-White syndrome, type B, tachycardias could reproducibly be initiated and terminated by a single electrically induced right atrial or right ventricular premature beat. This evidence further favours the presence of a right-sided bypass of the atrioventricular node as being responsible for the Wolff-Parkinson-White syndrome type B. However, up to this point, much of the evidence in favour of a corresponding left-sided relationship in type A has had to be inferential. While the evidence from Cases 3 and 11 was strong, further proof was desirable and this has now been provided by Wellens et al. (1971a) in five cases, and in a sixth case included in a brief report by the same workers (Wellens et al., 1971b).

In all patients, electrical stimulation was performed from the right side of the heart, and in three cases the effect of induced left-sided premature beats was also studied. In contrast to the ease with which paroxysmal tachycardias were initiated and terminated with premature beats injected into the right atrium or right ventricle in the type B syndrome, great difficulty was experienced with right-sided stimuli in type A cases. However, left-sided premature stimuli easily initiated and terminated paroxysmal tachycardias. They were also able to demonstrate that when paroxysmal tachycardia was induced, and simultaneous recording of right and left atrial activation was obtained during the tachycardia, the left atrium was activated earlier than the right, by 70-100 milliseconds. During these tachycardias the QRS complexes were narrowed, and it was thus possible to indicate a circus movement during the tachycardia, anterogradely down the atrioventricular node and bundle of His and retrogradely up the anomalous pathway into the left atrium. One patient however had the path of the tachycardia running in the reverse direction, i.e. anterogradely down the anomalous pathway and retrogradely at the bundle of His and atrioventricular node. The findings in this study indicate that in the Wolff-Parkinson-White syndrome, type A, the circus pathway is a left-sided one, because it can much more easily be stimulated and inhibited on the left side of the heart, and because during paroxysmal tachycardia it was possible to show retrograde early left atrial activation.

It was only in Case 5 that it was possible to induce an arrhythmia by right ventricular stimulation. In this case, however, the conduction was of the type A variety, and we here have the paradox that it was easy to induce paroxysmal tachycardia under these circumstances, yet this was achieved by <u>right</u> cardiac stimulation. This was one of the two patients with the Wolff-Parkinson-White syndrome who gave a history of paroxysmal tachycardia, and who was studied by His bundle electrography. Both were type A; and in one the arrhythmia was reproduced (see Chapter 8). Doubtless in Case 5 the stimulus crossed to the left and entered the bypass at the appropriate time. No conclusions should be drawn from the fact that stimulation in Case 1, with type B conduction, failed to produce an attack of tachycardia, because it was only in patients with type B syndrome who had a positive history of paroxysmal tachycardia that Durrer et al. (1967) found that they could reproduce this consistently.

Recently Boineau and Moore (1970) have modified the classification of Rosenbaum et al. (1945). They studied two patients with type B syndrome and a dog with type A syndrome; in all three cases pre-excitation occurred at the atrioventricular margin of the right ventricle as judged by epicardial mapping. In the patients with type B, the pre-excitation area was anterior whereas in the dog with type A it was posterior. These workers thus suggest that the right ventricle is always the location of entry of the pathway, but this can only apply to their cases, and the precise relevance of their dog study to man remains to be demonstrated. The fact that their hypotheses do not conform with the evidence cited above must make one hesitant to draw too many conclusions from their limited report; epicardial mapping is a difficult technique, and anatomical studies may show multiple pathways (Lev et al., 1955).

A careful study of a case of Ebstein's anomaly with Wolff-Parkinson-White conduction type B tends further to confirm the right-sided situation of the bypass (Watson and Lowe, 1967). Within the right ventricle intracavitary potentials showed a positive delta wave, which became negative as the electrode catheter was withdrawn into the atrialized right ventricle. This provides further evidence that the bypass activated an area of right ventricle between the atrioventricular annulus and the apex of the right ventricle.

According to the theory that the Wolff-Parkinson-White syndrome reflects the activity of an ectopic focus, in type A this was considered to be in the high posterior septal mass, and in type B it was thought to be in the right septal mass or free right ventricular wall (Sodi-Pallares et al., 1963). One could adapt the theory of synchronized sinoventricular conduction (Sherf and James, 1969), in those cases where it might conceivably turn out to be relevant, to suggest that fibres destined for the left ventricular myocardium show preferential conduction in type A, and vice versa in type B. However, as indicated in Chapter 2, the presence of anomalous pathways appears to have explained the Wolff-Parkinson-White syndrome in most if not all those cases where adequate anatomical studies have proved possible.

In type A, with conduction into the left ventricle, the mean front plane axis may be towards the right or the left. This, when conduction occurs down the bundle of His, respectively indicates (if the axis is pathologically deviated) conduction down the anterior or posterior division of the left bundle branch (depicted in Figure 28), and is caused by block of the other division (Krikler, 1971a). It seems logical that conduction down an anterior anomalous pathway will more easily fuse with conduction down the anterior division of the left bundle branch and produce a normal or right axis deviation, and that conduction via a posterior anomalous pathway would more easily fuse with concomitant conduction down the posterior division of the left bundle branch, causing left axis deviation. D. Durrer (personal communication) has also reasoned along these lines, but anatomical proof has not yet been sought. It may here be noted that normal or right axis deviation was present in Cases 3, 5, 11 and 12; left axis deviation occurred in Cases 4, 7 and 10.

In the final analysis, location of the site of an anomalous tract may require the study of endocardial and epicardial excitation. Confirmation by autopsy may likewise corroborate - or disprove - the deductions drawn, which do appear to strengthen the basis for the attribution of the tracts to either side of the heart on the basis of the electrocardiographic classification of Rosenbaum et al. (1945).

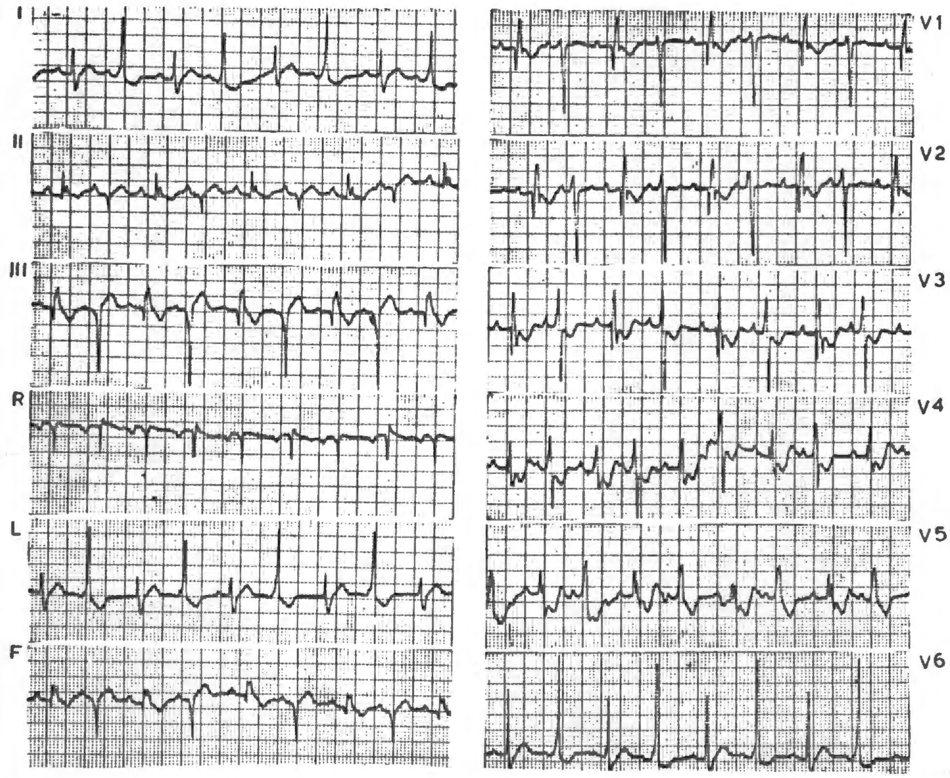


Figure 23 (Case 8) Electrocardiogram, showing right bundle branch complexes alternating with Wolff-Parkinson-White type B complexes.

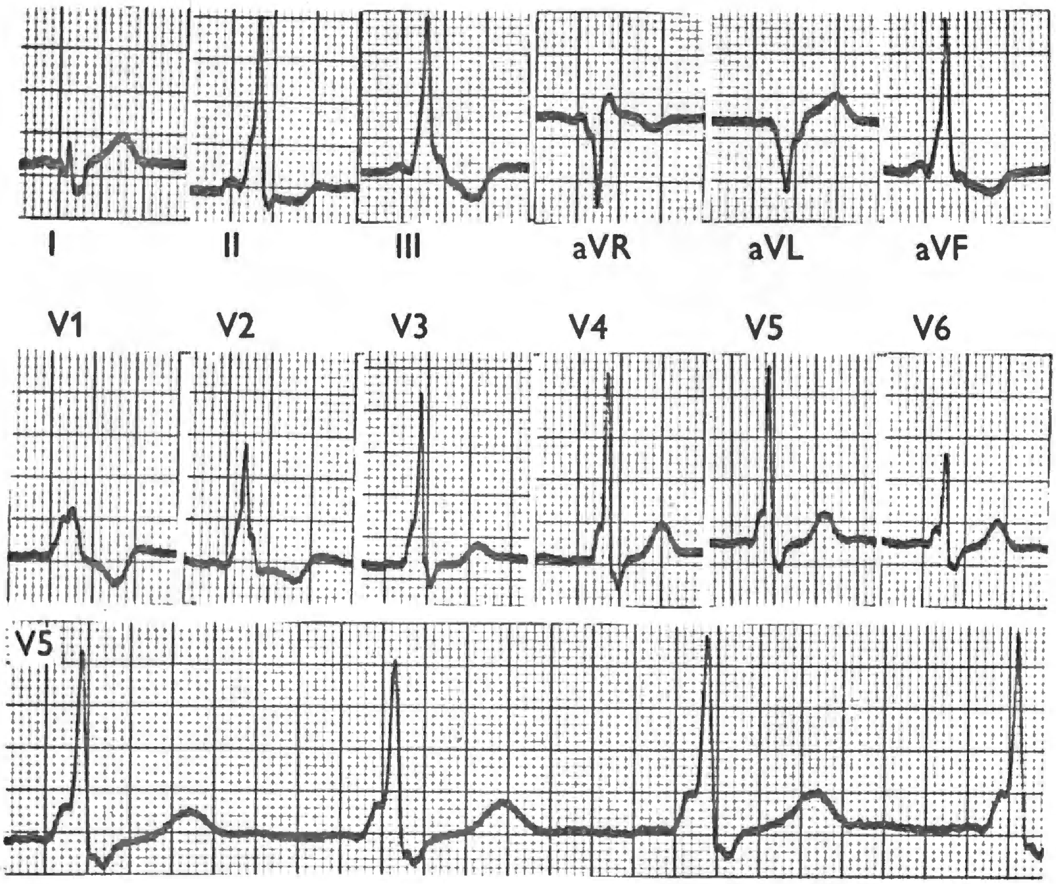


Figure 24 (Case 3) Standard electrocardiogram above; the bottom panel (V5) recorded at paper speed of 50 mm./second.

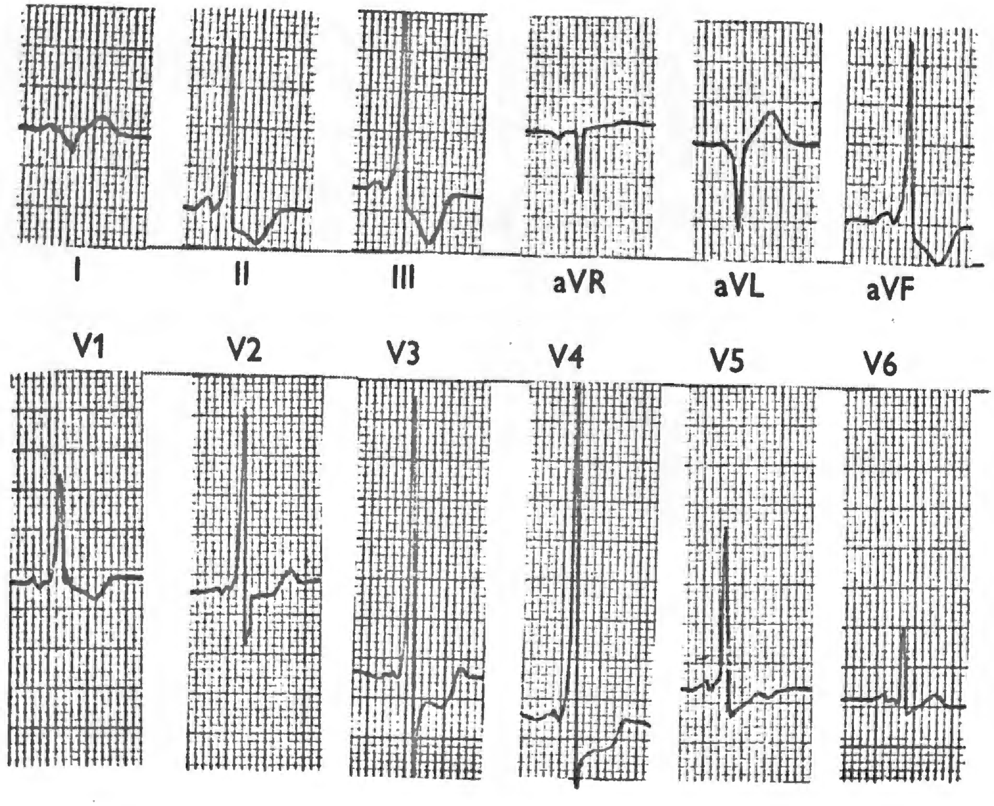


Figure 25 (Case 11) Electrocardiogram, immediately after conversion to sinus rhythm (100 beats a minute).

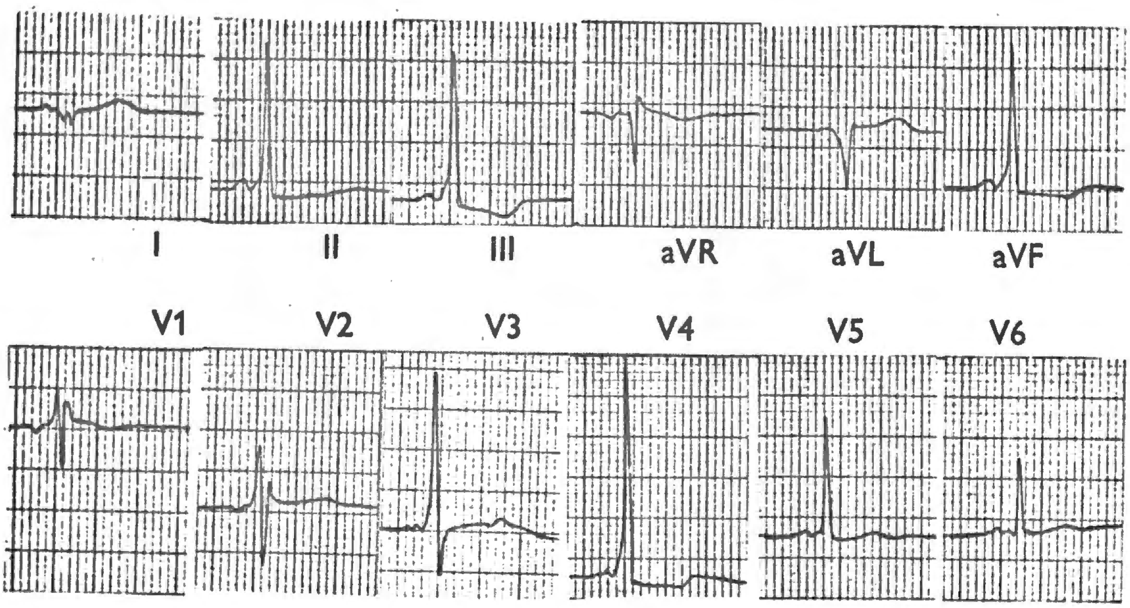


Figure 26 (Case 11) Electrocardiogram, one day after attack of paroxysmal tachycardia. (Heart rate 70 beats a minute).

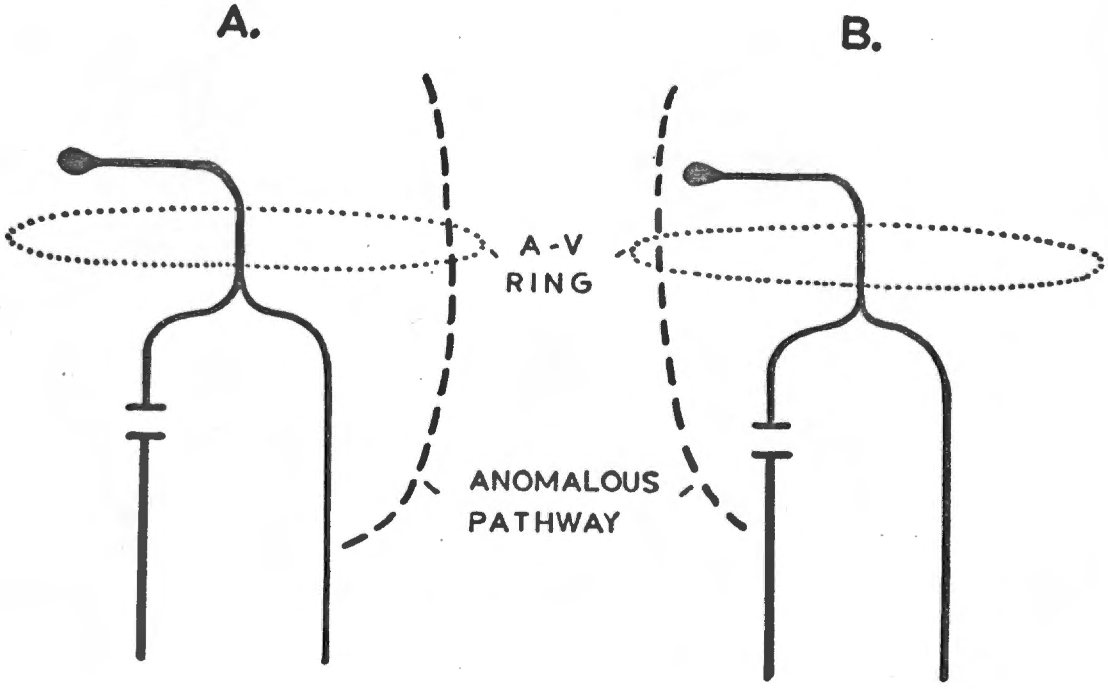


Figure 27 Diagram showing conduction pathways in Wolff-Parkinson-White syndrome, types A and B, with right bundle branch block.

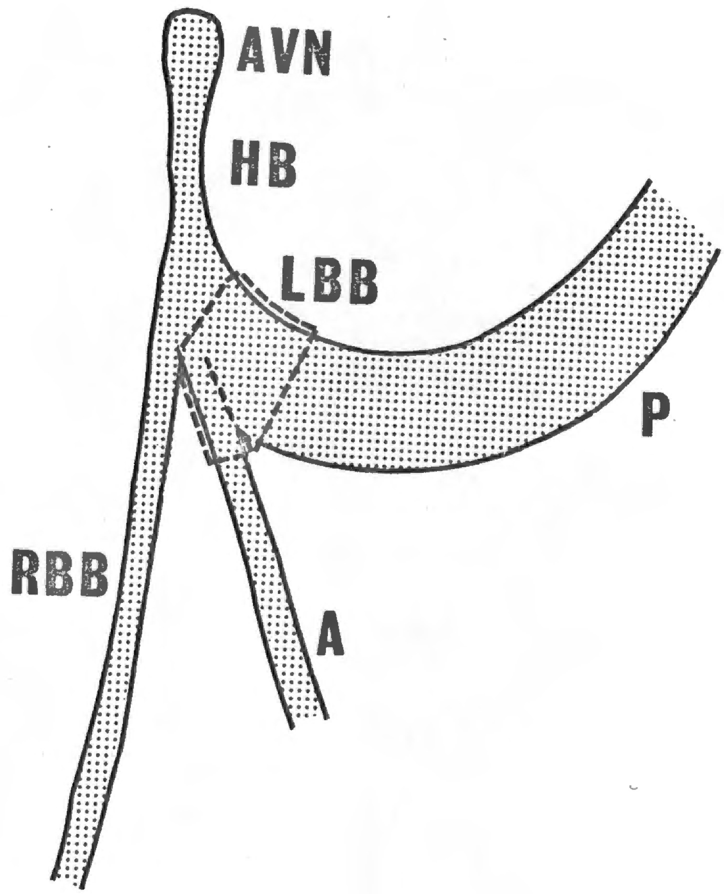


Figure 28 Diagram showing atrioventricular node (AVN), bundle of His (HB), left bundle branch (LBB) and its anterior (A) and posterior (P) divisions, and right bundle branch (RBB).

CHAPTER 5

Selected Clinical and Electrocardiographic Features

Certain aspects of the Wolff-Parkinson-White syndrome will be discussed not only on the basis of the reviews and original references cited, but also from a personal analysis of 74 cases seen at random. Those areas considered to be of particular interest have been selected for consideration here.

Age.

Whether or not it is always recognized as such at first, the Wolff-Parkinson-White syndrome has been recognized in the past from neonatal life (Engle, 1952) and infancy (Richmond et al., 1948; Gleckler and Lay, 1952) up to old age (Hejtmancik and Herrmann, 1957). Among the present cases, the ages ranged from the newborn to 70; the distribution is shown in Table II. Of the 8 cases below 10, all had congenital cardiac lesions - in 4 cases the Ebstein anomaly, and corrected transposition of the great vessels, atrial septal defect, ventricular septal defect and aortic stenosis singly in the others; it was the cardiac lesion or an arrhythmia that brought the cases to notice. Case 8 was seen soon after birth because of a cardiac murmur. An interesting correlation in neonatal cases is suggested by Bhandhusavee

Table II

Age Range in Patients with the Wolff-Parkinson-White Syndrome

Age in Years	Number of Cases
0-10	8
11-20	4
21-30	29
31-40	14
41-50	9
51-60	6
61-70	4

et al. (1972): reviewing reported cases as well as 9 of their own, type B conduction tended to be associated with congenital cardiac disorders and to be persistent, whereas type A conduction was often unassociated with such lesions and tended to be transient. They come closest to diagnosing the Wolff-Parkinson-White syndrome at the earliest possible opportunity - two of their cases had intrauterine tachycardia. At the other end of the scale, there were relatively few patients over the age of 40; then the numbers declined sharply. In early and middle adulthood, electrocardiograms are often recorded to exclude a cardiac cause for chest pain (e.g. Cases 1, 2 and 6) or as part of a check-up or for life assurance (Cases 4 and 10), when the Wolff-Parkinson-White syndrome may thus be discovered incidentally; or the patient may have presented during an arrhythmia (e.g. Case 11) or give a history of paroxysmal tachycardia (e.g. Case 9). Only four cases were older than 60: three of these had arrhythmias (5, 7 and 12) and the oldest, aged 70, was discovered when a routine electrocardiogram was taken before cholecystectomy (Case 3). The paucity of elderly cases - at a stage of life when electrocardiograms are commonly performed because of suspected cardiac ischaemia or the presence of hypertension, or prior to major surgery - is suggestive of a relatively low incidence. One can only surmise that some sufferers, not known to have the Wolff-Parkinson-White syndrome, may have died suddenly from arrhythmias. Although Case 5 had suffered from paroxysmal tachycardia since the age of 17, it only became troublesome when he was over 60; Cases 7 and 12 likewise only developed paroxysmal tachycardia when over 60, and in the former the attacks were at times life-threatening. It may well be that the increased frequency of extrasystoles with advancing age (Simonson, 1972) may be hazardous, by inducing possibly fatal arrhythmias in the Wolff-Parkinson-White syndrome. Sudden death, even though investigated by autopsy, will not yield evidence of the Wolff-Parkinson-White syndrome without the most meticulous histopathological study (Davies, 1971).

In general, the prognosis of the Wolff-Parkinson-White syndrome is excellent in the absence of paroxysmal tachycardia; even then it is good, though some cases die suddenly, particularly if the ventricular rate is fast, especially in the presence of atrial fibrillation (Flensted-Jensen, 1970), when the danger of ventricular fibrillation may be great (Dreifus et al., 1971a). By contrast with the latter situation is the uneventful survival of Case 3 to the age of 70; doubtless there are many others like him who have never been identified as having the Wolff-Parkinson-White syndrome, and who remain in excellent health.

Sex.

It is generally stated that there is a male preponderance in the Wolff-Parkinson-White syndrome (Hejtmancik and Herrmann, 1957; Scherf and Cohen, 1964; Newman et al., 1966): roughly 60-70% of cases are male. The present experience is in keeping with this: 50 of the 74 patients were male.

Incidence.

It must be appreciated that a precise measure of the incidence of the Wolff-Parkinson-White syndrome is extremely difficult to obtain, and much caution is required in interpreting claims made on the basis of the frequency with which the syndrome is recognized in patients referred to hospital. Here one is obviously dealing with people in whom some cardiac disorder is at least suspected; and the same applies to those seen in private practice. Swiderski et al. (1962) found the incidence to be approximately 1 in 500 children referred for cardiac assessment. Averill et al. (1960) and, later, Hiss and Lamb (1962) have studied the incidence in healthy American men already admitted into the United States Air Force, and the latter series, in which more than 122,000 individuals were studied, yielded 187 cases of the syndrome; a frequency of 1.5 per thousand. This may be a slight understatement of the frequency in this particular group, because anomalous conduction tends to be intermittent (see Chapter 3). Thus what they report is likely to be a minimum, but still applying only to healthy males in the age group liable for military service. A community population study in depth, of both sexes and at all ages, with tracings recorded on several occasions, is essential before one can know the true frequency and more precise age and sex distribution of the syndrome. Even here the problem of intermittency must be recognized, and consideration given to the transient nature of type A conduction in the neonates reported by Bhandhusavee et al. (1972); for we do not know if or when anomalous conduction returns in them in later life.

To get an idea of the frequency of the disorder in hospital practice, all electrocardiograms taken at the Prince of Wales's Hospital for one year (1971) were personally reviewed. These totalled 3339; in 1913 these were their first records (at least at this hospital). Among these were 4 new cases of the Wolff-Parkinson-White syndrome. Three cases presented with paroxysmal tachycardia, and in one an electrocardiogram was taken when a history suggestive of paroxysmal tachycardia was elicited in a man referred for possible cardiac disease, who turned out not to have cardiac pain (Case 9). This series is too small to be meaningful, and does no more than point to factors that determine the selection of cases that are recognized.

<u>Heredity</u>

None of the cases reported here in detail to illustrate features of the syndrome gave family histories that indicated the likelihood that any members were affected, i.e. none were known to have the Wolff-Parkinson-White syndrome, and no members of the families were known to suffer from paroxysmal tachycardia; but a detailed survey was not attempted, and it is possible that some members might have revealed the presence of the Wolff-Parkinson-White syndrome had it been possible to study them. However, heredity does not appear to play a major role, nor to be a most obvious feature of the syndrome. The situation has been well reviewed by Harris (1970). Here mention must be made of the claim by Massumi (1967) that the Wolff-Parkinson-White syndrome may occur in familial fashion in association with cardiomyopathy. However, careful perusal of his tracings suggests that they did not indeed have the Wolff-Parkinson-White syndrome. As discussed in Chapter 13, there is good reason for believing that these are cases of hypertrophic obstructive cardiomyopathy with features resembling the Wolff-Parkinson-White syndrome.

Although there have been many claims that the Wolff-Parkinson-White syndrome may occur on a heredity basis, this requires careful consideration before it is accepted. Undoubtedly such cases do occur. There is one family reported by Öhnell (1944), in which four of six siblings suffered from this condition, and another in which five siblings of the family of ten had paroxysmal tachycardia; in two of these, features of the Wolff-Parkinson-White syndrome were present. It is interesting that one of these latter cases was the first to be reported where a left-sided atrioventricular muscular bypass was present, i.e. a left-sided bundle of Kent; but the mere fact of its presence is not, as suggested by Öhnell (1944) "obviously consistent with the signs of heredity." Öhnell (1944) indicated that he had found signs suggesting heredity in other cases of pre-excitation, but did not give the basis for this claim.

Harnischfeger (1959) encountered the syndrome in three generations of a family; the grandfather, father and identical twin siblings all had the Wolff-Parkinson-White syndrome, type B, and the male, but not the female, member of a pair of fraternal twins had the syndrome, type A. Warner and McKusick (1958) studied fourteen families, and these included 80 members other than the probands; in no cases did they find others to be affected by the Wolff-Parkinson-White syndrome.

Associated congenital cardiac lesions.

It has long been recognized that Ebstein's anomaly of the tricuspid valve is complicated by the Wolff-Parkinson-White syndrome type B: nearly 10% of cases are thus affected (Frau and Agostoni, 1959), though the proportions vary in different series, from 2 out of 32 cases (Simcha and Bonham-Carter, 1971) to 8 out of 55 (Kumar et al., 1971). Interestingly, in left-sided Ebstein's anomaly, associated with corrected transposition of the great vessels, the Wolff-Parkinson-White conduction has been type A (Schiebler et al., 1961). But a wide variety of lesions may occur, including various forms of transposition of the great vessels, and cyanotic congenital heart disease with Wolff-Parkinson-White syndrome thus does not always indicate that Ebstein's anomaly is responsible for the presentation (Bhandhusavee et al., 1972). Congenital lesions in the present series are indicated under "Age".

The arrhythmias seen in Ebstein's anomaly are by no means always associated with Wolff-Parkinson-White conduction (Kumar et al., 1971), but it might be instructive to study such cases in whom conduction looks normal, for possible evidence of "occult" or "concealed" Wolff-Parkinson-White syndrome (see Chapter 11).

Duration of electrocardiographic intervals.

The P-R interval is not universally short, nor the QRS always prolonged, in the Wolff-Parkinson-White syndrome, as inspection of the data in the 74 cases shows (tables III and IV). Shortening of the P-R (0.12 seconds or less in 70) is somewhat more frequent a feature than widening of the QRS (0.10 seconds or more in 57). This is roughly comparable as regards the P-R interval with the criteria laid down by Wolff (1954): he reported that in 85% of cases the P-R was less than 0.12 seconds, and that in the same proportion the QRS exceeded 0.10 seconds.

Types A and B.

There were exactly equal numbers of cases (37) in each category, thus contradicting the claimed rarity of the former (see also Chapter 4).

Cardiac infarction and the Wolff-Parkinson-White syndrome.

The bizarre changes seen in the Wolff-Parkinson-White syndrome are of importance in two ways with regard to the presence or absence of cardiac infarction

Table III

P-R Interval (Wolff-Parkinson-White Syndrome)

P-R interval (seconds)	Number of cases
0.08	28
0.09-0.10	22
0.11-0.12	20
0.13-0.14	2
0.15	1
(Complete heart block)	1

Table IV

QRS Interval (Wolff-Parkinson-White Syndrome)

QRS interval (seconds)	Number of cases
0.08-0.12	17
0.11-0.16	57

or ischaemia. On the one hand, the appearances may be misread as indicating cardiac infarction; on the other, they may hide the evidence for an infarct.

The electrical axis of the delta wave and the pattern of depolarization of the ventricle during anomalous conduction may be such that apparent Q waves may be produced, thus erroneously leading to the diagnosis of cardiac infarction. In most cases of the Wolff-Parkinson-White syndrome the mean frontal plane axis of the delta wave is at or about +15 degrees (Zao, et al., 1958); other characteristics of the delta wave have been discussed in Chapter 2. When the delta axis is deviated to the left (e.g. -10 to -75 degrees), one will see apparent "Q" waves simulating inferolateral cardiac infarction. On the other hand, right axis deviation of the delta wave (around +100 to 120 degrees) will cause "Q" waves to appear in leads I and aVL, and this could suggest anterolateral cardiac infarction. To the uninitiated, the deep "QS" waves in right precordial leads in type B Wolff-Parkinson-White syndrome might well lead to an erroneous diagnosis of anteroseptal cardiac infarction. In all patients with type A Wolff-Parkinson-White syndrome, the tall R wave may spuriously suggest the presence of true posterior cardiac infarction. Thus normalization may not be just an interesting exercise; it may need to be sought, whether occurring spontaneously or if inducible by appropriate measures (Chapter 3) in order to see what lies hidden by the cloak of Wolff-Parkinson-White conduction.

The features in individual cases where a mistaken diagnosis of cardiac infarction could be - or indeed was - made are set out in table V. It may be argued that in some of these cases the resemblance to cardiac infarction is slight, and the criteria for the diagnosis of infarction were not properly met, and this is fully conceded. Yet often the diagnosis of cardiac infarction has to be made or considered when the electrocardiogram is not fully typical; this is where an inexperienced observer may be caught out, misdiagnosing the Wolff-Parkinson-White syndrome as representing cardiac infarction. Thus Cases 1, 2, 4, 6 and 7 were seen in the normal way at hospitals to which they were referred for symptoms thought possibly to be cardiac, and the electrocardiogram in each case was initially misread as confirming

Table V

Simulation of Cardiac Infarction

by the Wolff-Parkinson-White Syndrome

Case	Figure	Type	"Q" in leads:-	"Location of infarct"
1	6	B	V1	Anteroseptal
2	11	B	III, aVF, V1	Inferolateral ± Anteroseptal
3	24	A	aVL (I)	Anterolateral
4	16	A	III	Inferior
5	8	A	I, aVL	Anterolateral
6	3	B	III, V1	Inferior ± Anteroseptal
7	9	A	III, aVF	Inferolateral
9	4	B	II, III, aVF	Inferior
11	25	A	I, aVL	Anterolateral

the presence of cardiac infarction. Conversely, once the Wolff-Parkinson-White syndrome had been diagnosed in Case 7 it was only during pseudo-normalization that possible genuine evidence of cardiac infarction could be evaluated (Figure 10). According to Wolff (1954), Q waves do not occur in the left precordial leads in the Wolff-Parkinson-White syndrome, but this can clearly not be the rule during partial normalization. Indeed, Wolff (1954) has published tracings in which evidence of anterior cardiac infarction could only be seen during normal conduction, and not when conduction was anomalous. Further examples of this sort are reviewed by Scherf and Cohen (1964). The problems here may therefore be summarized that a negative delta wave in V1 may produce a spurious Q suggesting localised antero-septal infarction; negative delta waves in leads II, III, or aVF may produce similar changes leading to the diagnosis of inferior infarction; tall right precordial R waves (type A) may suggest true posterior infarction and loss of the Q wave because of the supervention of a positive delta wave may hide the signs of an infarct (Wolff, 1954; Grayzel, 1958).

The S-T segment and T wave abnormalities that are so commonly present in the Wolff-Parkinson-White syndrome are of no diagnostic value in pointing to cardiac ischaemia and should not be misinterpreted as being additional evidence of myocardial infarction in patients who suffer from this syndrome (Wolff and Richman, 1953; Bleifer et al., 1959). It is impossible to assess the extent to which the S-T segment and T wave changes in Case 7 reflected underlying ischaemia, but noteworthy that there was more clear evidence of T inversion in leads I and V4-6 during partial normalization (Figure 10); this is possibly important evidence of ischaemic damage, for the greater the degree of pre-excitation, the more marked the ST-T changes (Öhnell, 1944).

One of the few instances where cardiac infarction can positively be diagnosed in the presence of consistent pre-excitation is seen in the case cited by Sodi-Pallares et al. (1963): the R waves were seen to decrease across the precordium from right to left, and at autopsy, old cardiac infarction was found. Another way of seeking evidence of infarction is provided by the fortuitous occurrence of ventricular extrasystoles; the morphology of these extrasystoles may be conclusive (Bisteni et al., 1961). The configuration of QRS complexes in unipolar leads should be of the QR, qR or qRs - but not the QS - type, since the QS pattern can normally be found near the site of origin of ventricular extrasystole. This can be applied to extrasystoles occurring in patients with the Wolff-Parkinson-White syndrome, and is clearly exemplified in Case 7 (Figure 29 - V3-V6; see also leads I and aVL). This provides support for the evidence suggestive of cardiac infarction seen in Figure 10. It may well be that his paroxysmal arrhythmias precipitated cardiac infarction, most likely in association with underlying coronary arteriosclerosis.

In Cases 1, 2 and 10, when QRS complexes showed normal conduction, there were inverted T waves in certain leads, e.g. Case 1: III and aVF; Case 2: II, III, aVF and V6; Case 10: II, III and aVF. The explanation for this is not clear, but in none is there evidence of underlying heart disease. These include leads (III) in which inverted T waves occur without pathological significance, but the inversions are more extensive than this. Whether there is some minor concomitant concealed pre-excitation (in the sense defined by Öhnell, 1944, as almost complete normalization) is conjectural; but it is plausible that repolarization is minimally and visibly affected thereby, with the changes seen in these cases.

Bundle branch block.

The association of bundle branch block is of especial interest in the light of the location of the pre-excitation areas (Chapter 4). Of the 74 cases examined, right bundle branch coexisted with the Wolff-Parkinson-White syndrome type B in 9 cases, but in all but one of these the pattern of pre-excitation alternated with the pattern of right bundle branch block, i.e. the right bundle branch block normalized the Wolff-Parkinson-White conduction. In the presence of an anomalous pathway of the Kent type, the normal conduction system is bypassed away from the intraventricular septum, and as indicated above, this normalization is to be expected. Persistence of both patterns is thus suggestive of the presence of an anomalous pathway inserted into the ventricle or conducting tissue proximally, viz early in the course of the right bundle branch, before the area of the block. This would therefore suggest the presence of a Mahaim tract rather than the bundle of Kent. Indeed, this was the pathological finding in one such case (Lev et al., 1966), and might explain the findings in the cases reported by Bellet (1971) and Zakopoulos et al. (1964). However, in the majority of these affected, according to published reports, right bundle branch block tends to alternate with Wolff-Parkinson-White syndrome type B (Bleifer et al., 1959; Durrer et al., 1967; Gersony and Ekery, 1969; and Richmond and Pordy, 1969).

In four cases right bundle branch block co-existed with Wolff-Parkinson-White conduction type A and one would not have expected otherwise if the bypass is left-sided, as it is in type A. Examples of this association are Cases 3 and 11. Left bundle branch block occurred in three cases, all type B, i.e. with presumed right-sided bypasses.

The occurrence of right bundle branch block only during supraventricular tachycardia complicating a case of Wolff-Parkinson-White syndrome, type B (Bleifer et al., 1969) is not really relevant, for here the conduction is anterograde down the normal pathway, and one is dealing with the common situation of aberrant conduction due to functional block in the right bundle branch because of the tachycardia (Sandler and Marriott, 1965).

The true frequency of right bundle branch block complicating the Wolff-Parkinson-White syndrome type A is not known. Two aspects arise which merit further consideration as to which is primary:-

(a) If pathological damage to the conduction tissue favours diversion of the impulse leading to ventricular depolarization into the anomalous pathway (and here the findings of De Mesquita, 1955, bear thought), right bundle branch block might "open up" the anomalous pathway in this manner. This is unlikely in the absence of some damage to the left bundle branch or its anterior and posterior divisions, as these tracts could be expected to conduct preferentially, more so than the anomalous pathway. However, if this were possibly part of the explanation, the development of manifest right bundle branch block (perhaps the first detectable electrocardiographic evidence of more extensive bundle branch disease) might be another explanation for "acquired Wolff-Parkinson-White syndrome" late in life.

(b) Left-sided anomalous conduction may leave "too little" of the impulse to traverse the right bundle branch; i.e. there might now be a mismatch impedance between the right bundle branch and the right ventricular mass. This would become electrocardiographically manifest as right bundle branch block. Indeed, Case 11 showed an inverse relationship between the degree of anomalous conduction and the degree of right bundle branch block, i.e. the more conduction down the right bundle branch, the less the pre-excitation, and vice versa.

The infrequency of reported cases of the association of the Wolff-Parkinson-White syndrome and left bundle branch block (Castellanos et al., 1962; Varriale et al., 1966) makes similar comparisons difficult. The role of damage to the normal conducting tissue in relation to the expression of the Wolff-Parkinson-White syndrome clearly requires further clarification.

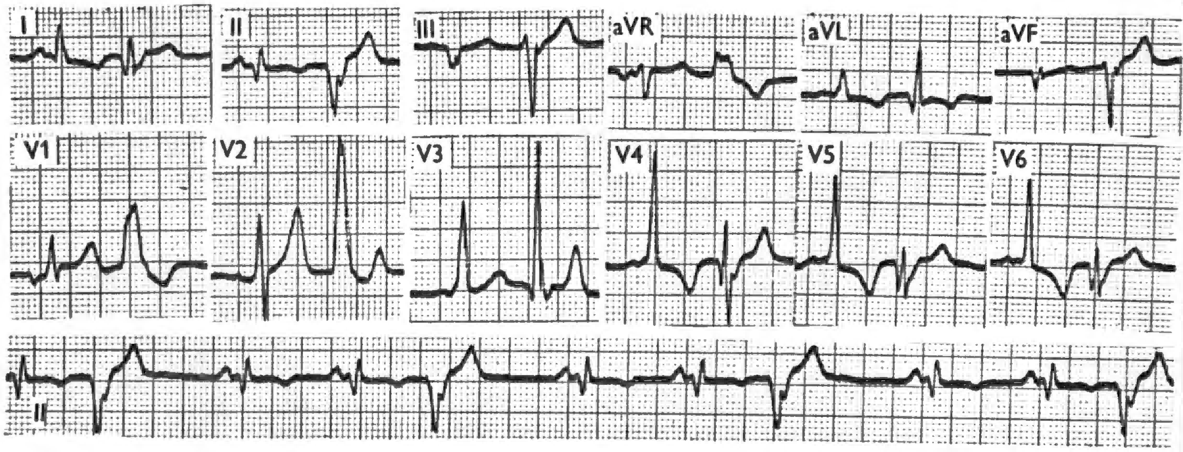


Figure 29 (Case 7) Electrocardiogram showing unifocal ventricular extrasystoles.

CHAPTER 6

His Bundle Electrography and the Wolff-Parkinson-White Syndrome

The development of techniques for recording potentials from the conducting tissue of the human heart by means of intracardiac electrodes have provided the opportunity to explore in greater detail and with greater precision abnormalities in a wide variety of disturbances of cardiac rhythm and conduction. Giraud et al. (1960) first showed that it was feasible to insert an electrode catheter into the heart during pervenous cardiac catheterization, and were able to define the characteristics of impulses recorded from the atrioventricular node and from the bundle of His. Watson et al. (1967) were less successful in recording such activity; in more than 700 patients with congenital or acquired lesions subjected to cardiac catheterization with careful exploration with electrode catheters, they failed to register such recordings. The only patient in whom they succeeded was in a 14-year-old girl with Ebstein's anomaly of the tricuspid valve, in whom the electrocardiogram did not have the appearances of the Wolff-Parkinson-White syndrome; their findings in this case conformed with those of Giraud et al. (1960). Scherlag et al. (1969) further developed the technique, and showed that by positioning the catheter properly so that the electrodes lay in the area of the tricuspid valve, and with appropriate amplification and filtering of the frequency of the impulses, reliable recordings could be obtained of the His bundle potentials, shown as a biphasic or triphasic deflection between the atrial and ventricular electrograms. These methods have been applied in particular to the analysis of the atrioventricular conduction defect in various types of heart block (Narula et al., 1970a; Narula et al., 1970b; Narula et al., 1971). Damato and Lau (1970), Rosen (1971), Smithen and Sowton (1971) and Smithen et al. (1971) have reviewed the value of the technique clinically and its usefulness in the study of the effect of various therapeutic agents on the conduction tissues. Narula et al.(1970c) have also recorded electrograms on the left side of the heart by retrograde arterial catheterization and positioning the catheter tip to lie in the region of the aortic valve close to the tip of a right-sided catheter apposed to the bundle of His in the usual way. By simultaneous recordings from the left and right catheters they were able to confirm that they were indeed recording the bundle of His activity from the left side of the heart.

His bundle electrograms were recorded in three patients with the Wolff-Parkinson-White syndrome (Cases 1, 5 and 7). Patients with other disorders were investigated in the same manner and the findings in them are reported in Chapters 7, 9, 11 and 12. All patients were studied in the supine position at rest without premedication and informed consent was obtained in each case. The His bundle electrogram was recorded via a bipolar electrode catheter (United States Catheter Incorporated) introduced into the femoral vein and positioned across the tricuspid ring under fluoroscopic control (Smithen and Krikler, 1972). His bundle potentials were recorded over a frequency band of 40-500 cycles per second (Herz) (HBE lead); the catheter position was adjusted until a sharp biphasic deflection appeared between the P wave and QRS complex of a standard lead electrocardiogram recorded simultaneously. The recordings were made with a Cambridge six channel photographic unit at a paper speed of 100 mm/second.

A second bipolar electrode catheter was then introduced through an arm vein, advanced to the junction of the right atrium and superior vena cava, and used to pace the atrium with a Multitone external battery-powered pacemaker. The following measurements were made. The P-R interval (representing intra-atrial, atrioventricular nodal, and intraventricular conduction times) was measured as in conventional electrocardiography. The P-H interval (representing atrial and atrioventricular nodal conduction) was measured from the beginning of the P wave or pacing stimulus to the beginning of the His potential. The H-Q or H-V interval (representing intraventricular conduction) was measured from the His potential to the onset of ventricular depolarization in the standard lead (H-Q), or to the onset of the ventricular deflection in the His bundle electrogram (H-V). The A-H interval (representing the time between low right atrial and His bundle activation) was measured in one patient from the onset of the atrial potential in the His bundle electrogram to the His deflection. The normal values in sinus rhythm, obtained previously on ten patients without atrioventricular conduction abnormalities, agreed well with those established in the literature: delays of 80-140 Msec. for the P-H interval, and 35-55 Msec. for the H-Q interval were considered normal (Smithen and Sowton, 1971). The broad relationships of these intervals to the electrocardiogram is shown schematically in Figure 30, and in greater detail in Figure 31, from the paper by Damato and Lau (1970).

<u>Case 1.</u> During sinus rhythm, the electrocardiogram showed consistent pre-excitation, with a normal P-H and a short H-Q interval (Figure 32, left panel). With right atrial pacing at progressively faster speeds (Figure 32, middle and right panel), the P-H interval increased in duration in physiological fashion, but the H-Q time remained unchanged (table VI).

<u>Case 5.</u> A tracing taken during sinus rhythm showed little evidence of pre-excitation on the electrocardiogram, and this was confirmed by the normal P-H and H-Q intervals on the His bundle electrogram (Figure 33; table VII). Atrial pacing with progressive reduction of the cycle length resulted in the expected prolong-

Table VI

Case 1, His bundle electrogram

Heart rate (Beats/minute)	Cycle length (R-R, milliseconds)	P-H (milliseconds)	H-Q (milliseconds)
70 (sinus)	850	85	15
97 (paced)	620	120	15
136 (paced)	440	140	15

Table VII

Case 5, His bundle electrogram

Heart rate (Beats/minute)	Cycle length (R-R, milliseconds)	P-H (milliseconds)	H-Q (milliseconds)
88 (sinus)	680	55	40
116 (paced)	515	110	30
136 (paced)	440	140	25
154 (paced)	390	165	0

ation of the P-H and A-H intervals, but the H-Q interval decreased progressively, and at a cycle length of 390 milliseconds, there was simultaneous activation of the His bundle and ventricular chamber, with a change in the QRS configuration on the electrocardiogram (Figure 34; table VII).

Case 7. In sinus rhythm there was little evidence of pre-excitation on the electrocardiogram; His bundle potentials are clearly seen and the P-H H-Q intervals were normal (Figure 35; table VIII).

As the cycle length was progressively decreased by atrial pacing, pre-excitation became more evident (Figure 36; table VIII). The P-H interval lengthened progressively, and the H-Q interval became shorter. When the cycle length reached 355 milliseconds the H-Q interval was 0. The simultaneous electrocardiograms showed progressively increasing pre-excitation, with a relatively normal-looking electrocardiogram at a cycle length of 570 milliseconds; the emergence of a rudimentary delta wave on the upstroke of R at 400 milliseconds; and a very definite delta wave at 355 milliseconds.

Table VIII

Case 7, His bundle electrogram

Heart rate (Beats/minute)	Cycle length (R-R milliseconds)	P-H (milliseconds)	H-Q (milliseconds)
74 (sinus)	780	90	50
105 (paced)	570	130	40
150 (paced)	400	140	15
180 (paced)	355	145	0

Figure 37 shows the appearances during sinus rhythm without pacing, in which normal conduction (first and third complexes) alternated with pre-excitation (second and fourth complexes). Although no obvious P waves are visible on the electrocardiogram, the H-H interval is regular, and extrasystoles are thus excluded. The H-Q interval is 15 milliseconds in the relatively normal complexes, but is 0 for all those showing pre-excitation. Spontaneous change to pre-excitation was therefore associated with greater shortening of the H-Q interval to the point at which simultaneous activation of the bundle of His and the ventricular chamber could be demonstrated.

During sinus rhythm, at a time when conduction showed little evidence of pre-excitation, occasional extrasystoles were noted, and a tracing that includes one is shown in Figure 38. On the electrocardiogram, this is suggestive of a ventricular extrasystole, but it is necessary to rule out the possibility of a supraventricular extrasystole with aberrant conduction. The absence of a preceding His bundle deflection clearly shows its ventricular origin.

This is in keeping with the ventricular extrasystoles diagnosed electrocardiographically (Figure 29); further consideration of the possible role of ventricular extrasystoles in the production of paroxysmal tachycardia will appear in Chapter 8. This may be of importance in the prevention of arrhythmias (Chapter 10).

Discussion.

Two important implications arising out of His bundle electrography in relation to pre-excitation are that an unduly short P-H time suggests the operation of a tract bypassing the atrioventricular node, and that an unduly short H-Q time implies supraventricular stimuli reach the ventricles through a bypass that short-circuits the bundle of His. Classifications of pre-excitation have been worked out using these points, as the basis for deduction of pathways operative in specific cases (Castellanos et al., 1971a; Coumel et al., 1971b, and 1972), and this aspect will receive further consideration later.

Cases 1, 5 and 7 are examples of the classical Wolff-Parkinson-White syndrome in that they all have short P-R intervals, delta waves and wide QRS complexes, and all three of them show varying degrees of pre-excitation at different times. Observations using His bundle electrography in these patients are consistent with the hypothesis that ventricular pre-excitation results from a bypass of the main bundle of His, since they all demonstrated QRS complexes formed by fusion between the normal and premature activation processes. During sinus rhythm or atrial pacing, when the pre-excitation pattern was seen, the His bundle deflection occurred simultaneously with the QRS complex or preceded it by less than 15 milliseconds. As the lower limit of normal for the H-Q interval is 35 milliseconds in sinus rhythm and remains unchanged during atrial pacing (Damato and Lau, 1970), the simultaneous activation of the bundle of His and occurrence of the QRS complex implies early activation of the ventricle, that is, earlier than could be expected via the normal route. None showed ventricular activation preceding the onset of the His bundle potential although this has been found in some cases (Castellanos et al., 1970). This may have implications as to which bypasses are involved (Castellanos et al., 1971a).

As the atrioventricular nodal conduction time became prolonged during atrial pacing, with progressively shorter cycle lengths, there was often an increasing degree of pre-excitation, with less of the conduction occurring via the bundle of His. It might have been anticipated that total activation would have occurred through the bypass had pacing been carried out at rates sufficiently fast to render the atrioventricular node totally refractory. As has been shown by Durrer et al. (1967), there is a critical point about which the atrioventricular node demonstrates physiological second-degree block, but in this case this was not reached. The changes noted in these cases, with the increasing amount of pre-excitation occurring with more rapid pacing, provide evidence that preferential conduction down a bypass will be favoured because the atrioventricular node becomes physiologically blocked; and when that stage is reached, the bypass is the only channel whereby the impulse can enter the ventricular chamber.

In recent years there has been valuable work on this topic. The findings of Castellanos et al. (1970) in two patients with the Wolff-Parkinson-White syndrome studied with His bundle electrograms are instructive. In the first case, a 62-year-old man with a history of paroxysmal rapid heart action for 50 years (who incidentally had a son with the Wolff-Parkinson-White syndrome and paroxysmal tachycardia), the electrocardiogram showed the Wolff-Parkinson-White syndrome type A. The first tracings obtained during His bundle electrography were recorded in sinus rhythm at a rate of 50 beats a minute. The P-R interval was 130 milliseconds, and the P-H interval 100 milliseconds; by subtraction the H-R interval (more usually expressed as the H-Q) was 30 milliseconds. Thus although the three standard limb leads appeared to show normal atrioventricular conduction, H-Q interval was just below the lower limit of normal, being 30 instead of 35 milliseconds. With atrial pacing at progressively faster rates, both P-R and P-H intervals became longer, as is usual in patients who do not have the Wolff-Parkinson-White syndrome (Castellanos et al., 1971a). Anomalous atrioventricular conduction only developed when the atrial pacing rate rose to 90 beats a minute, and at this stage a delta wave could be seen in the electrocardiograph leads. The P-R interval was the same, 200 milliseconds, during pacing at 60 beats a minute, as at 90 beats a minute, but the P-H interval increased from 140 to 190 milliseconds. By subtraction the H-Q interval was extremely short, 10 milliseconds. Further proof of early depolarization of the ventricles was obtained by pacing at faster rates, 100 and 125 beats a minute, when the P-R interval did not change but the P-H interval lengthened to 230 and 250 milliseconds respectively; at these rates the His bundle deflection now occurred after the onset of ventricular depolarization as judged from the extremity leads. Concomitantly the QRS complexes became wider. With atrial pacing at 145 beats a minute, the QRS complexes were now even more distorted and widened, and the His bundle deflection could not be identified. The evidence thus favoured total activation of the ventricles through a bypass, with no contribution down the bundle of His; but between 90-125 beats a minute, the complexes were intermediate, suggesting that, while the major activation took place through the bypass, some was still transmitted through the bundle of His.

In the second patient studied by these workers, a 36-year-old woman who had suffered from palpitations for ten years, the Wolff-Parkinson-White syndrome type A was diagnosed from the electrocardiogram. In sinus rhythm there was spontaneous variation in the degree of pre-excitation between two consecutive beats, which was clearly visible on the electrocardiogram, the second beat showing greater QRS widening and a more distorted complex. The P-H interval was similar in both beats but the P-R interval was shorter in the second beat, in which the His bundle deflection appeared 10 milliseconds after the beginning of the QRS complex, thus showing that some part of the ventricles was excited before the impulse could arrive down the bundle of His. With atrial pacing the response was very similar to that in the first case described.

Castillo and Castellanos (1970) made further studies on three patients with the Wolff-Parkinson-White syndrome, type A, including one already discussed in Castellanos et al. (1970). They suggested that, when the His bundle deflection can be seen on pacing to follow the onset of ventricular depolarization, one may be dealing with total bypass of the normal atrioventricular junction; what they describe as an "electrophysiologic" bundle of Kent without necessarily implying a specific anatomical location. Their third case always had a visible His deflection prior to the onset of ventricular depolarization, and they used this finding to imply the possible activation of the ventricles early through an infranodal preferential pathway (Mahaim fibre).

In this patient, during sinus rhythm without pacing, the P-H interval was 120 milliseconds at all times. With normal beats, the P-H interval was 175 milliseconds, and the H-R interval, of 55 milliseconds, was not widened. This is to be contrasted with the appearances during spontaneous Wolff-Parkinson-White beats in which the P-H interval was unchanged but the H-R interval extremely short, at 10 milliseconds: this gives a somewhat short P-R interval of 130 milliseconds, and the QRS complex was considerably widened at 140 milliseconds.

Intermediate beats were seen with the same P-H interval, but an H-R interval of 40 milliseconds and a P-R interval thus totalling 160 milliseconds; the QRS complexes were intermediate in width (100 milliseconds) and in appearance, with small delta waves, but without the more obvious appearance of the Wolff-Parkinson-White syndrome. The conclusion drawn by Castillo and Castellanos (1970) was that these latter beats reflected conduction down a Mahaim fibre, and they quoted the criteria laid down for this by James (1969). These are the presence of early ventricular (septal) excitation, a slight degree of (initial) QRS distortion, and an isoelectric interval between the end of the P wave and the onset of ventricular depolarization. An alternative explanation is that there are different degrees of pre-excitation; none during the normal beats, maximal or almost maximal during the Wolff-Parkinson-White beats, and intermediate during those beats said to be representative of Mahaim fibres, where the degree of normal and premature excitation was intermediate between the first two situations.

More recently Castellanos et al. (1971a) have expanded this approach and have attempted, on the basis of physiological behaviour during intracardiac electrography, in sinus rhythm and with atrial pacing, to localize the anomalous pathways in pre-excitation syndromes.

These workers postulate that the Wolff-Parkinson-White syndrome due to conduction down the bundle of Kent can be recognized by the following criteria. During sinus rhythm, the P-R interval is short, and the atrioventricular nodal conduction time normal. They identify the P-R interval as the time between a deflection produced by depolarization of the low right atrium and that of the ventricle, and the atrioventricular conduction time as the interval between low right atrial and bundle of His deflection. During atrial pacing, the interval between the stimulus and ventricular depolarization remains unchanged, but the normal atrioventricular nodal delay occurs and the interval between low right atrial activation and the bundle of His deflection becomes prolonged, so that the bundle of His deflection may be delayed and occur only after the R wave.

With Mahaim bundles responsible for pre-excitation, the time between the bundle of His deflection and the ventricular deflection will, they say, be shortened because of faster infranodal conduction. This would not be expected to change with right atrial pacing because of the interposition of the atrioventricular node, which will experience physiological delay, and project any reflection of its effects on the infranodal bypass.

A James bundle should produce shortening of the P-R interval only; this will be due to a decrease in the time between low right atrial activation and the bundle of His deflections. With atrial pacing, this interval will not increase until such time as the refractory period either of this particular bundle, or of the atria, is reached.

With a combination of James and Mahaim bundles (Lev et al., 1966) the ordinary electrocardiogram can be expected to show P-R shortening and QRS widening and distortion, in exactly the same way as with anomalous conduction through a bundle of Kent. However, atrial pacing need not produce an increase either in the interval between low right atrial activation and activation of the bundle of His, or in the duration of the ventricular complexes.

A word of caution must be expressed before these elegant deductions are extrapolated to the prediction of exactly what one is likely to find in the human being suffering from the Wolff-Parkinson-White and Lown-Ganong-Levine syndromes. As Castellanos et al. (1971a) agree in some of their illustrations, they do not always have necropsy evidence to support these deductions. It is obviously highly desirable for there to be more necropsy studies performed on patients who have undergone careful electrophysiological investigation, when they die, if this is at all feasible. Only in this way, can these interesting hypotheses be correlated with real situations. The same must apply to the synthesis proposed by Coumel et al. (1971a, 1971b), and in particular to their very elegant and logical explanation for the occurrence of the Wolff-Parkinson-White syndrome with narrow QRS on the basis of conduction via James and Mahaim fibres <u>in parallel</u> (e.g. Case 12; see Figure 5):-

1. Rapid activation by the James bundle (posterior internodal tract) partly or completely corrects the ventricular pre-excitation by the bundle of Kent;
2. Such cases have short P-H time, and the H deflection precedes the delta wave;
3. The delta wave is enlarged and the QRS is widened, and the H deflection delayed, by suitably timed atrial extrasystole;
4. Rapid reciprocal rhythm has occurred in these cases, suggesting the use of anomalous tracts in both directions; and
5. The delta wave increased when the James fibres were cut in one case.

Thus while much has been learned from His bundle electrography in the Wolff-Parkinson-White syndrome, the answers derived have posed even more questions. Further studies along these lines are necessary - and anatomical corroboration essential.

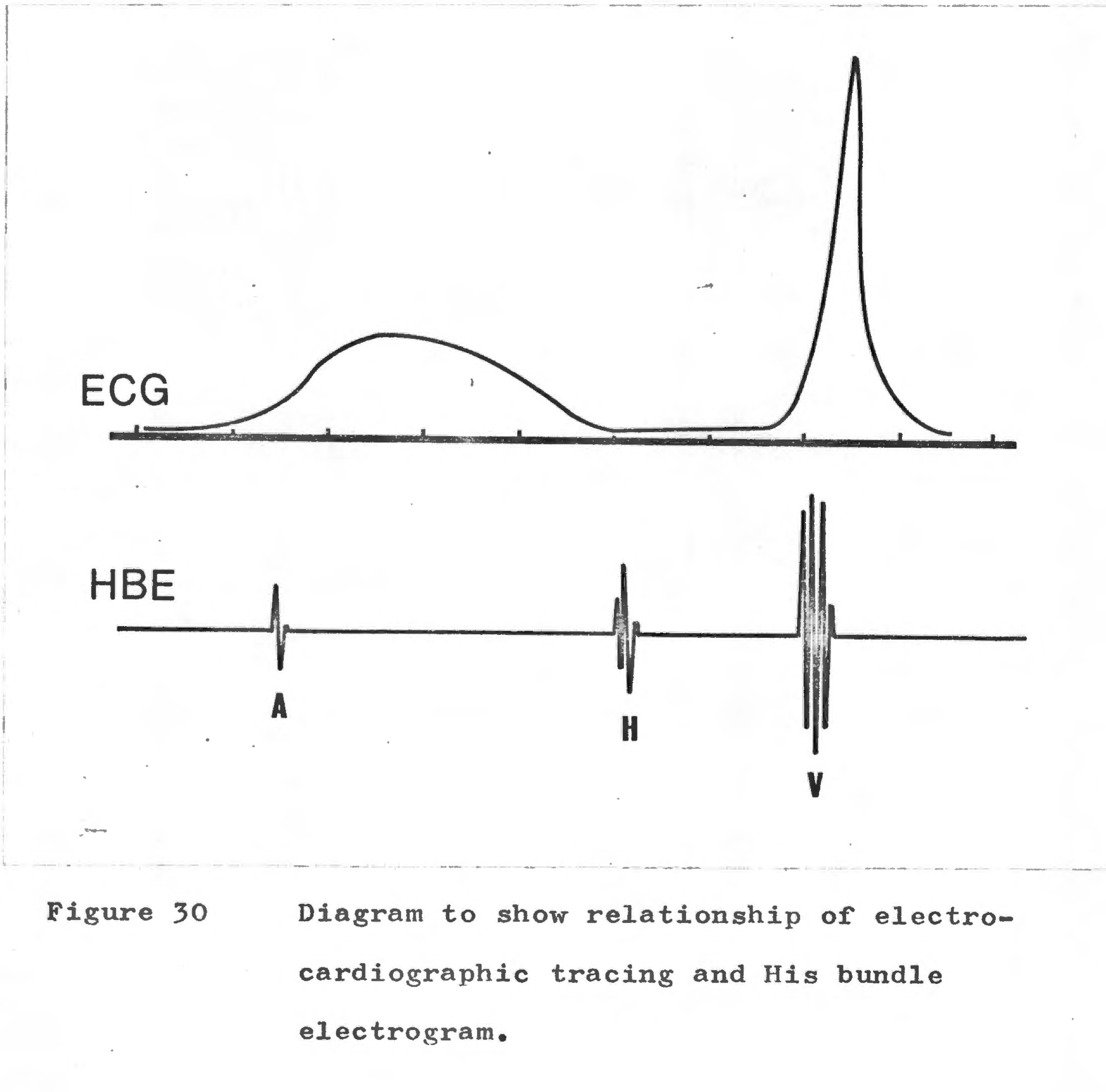


Figure 30 Diagram to show relationship of electrocardiographic tracing and His bundle electrogram.

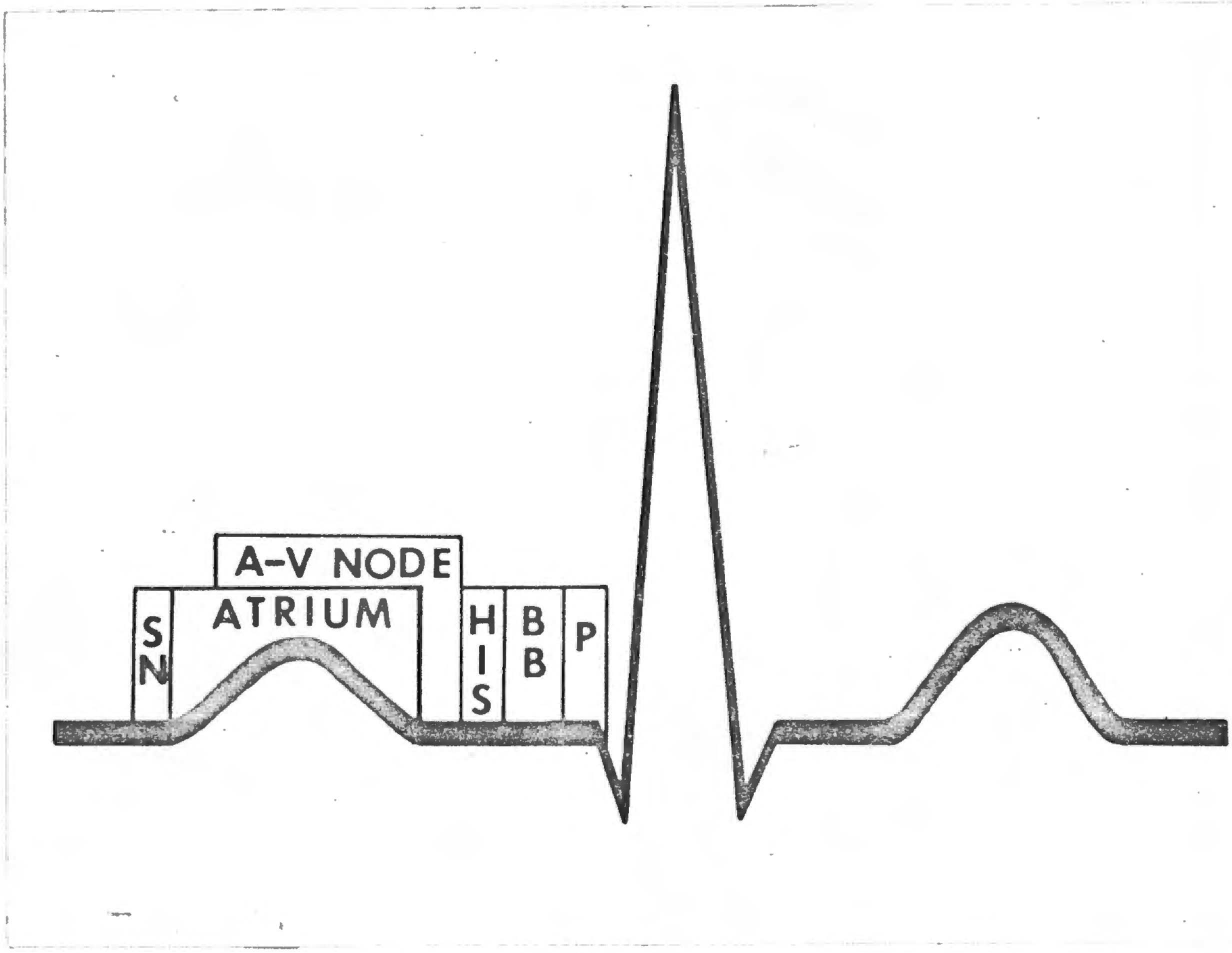


Figure 31 Diagram showing relationship of intra-cardiac conduction and depolarization to P-R interval of electrocardiogram. SN = sino-atrial node; His = bundle of His; BB = bundle branch. (From Damato and Lau (1970).

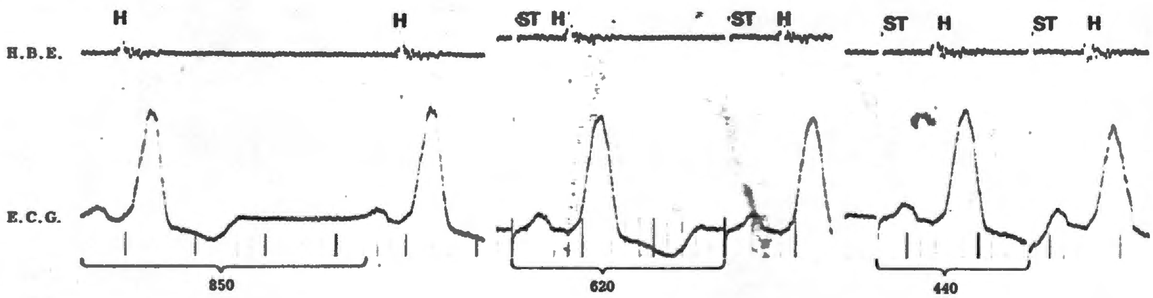


Figure 32 (Case 1) Simultaneous His bundle electrogram and electrocardiogram, in sinus rhythm (left panel) and during right atrial pacing (right two panels).

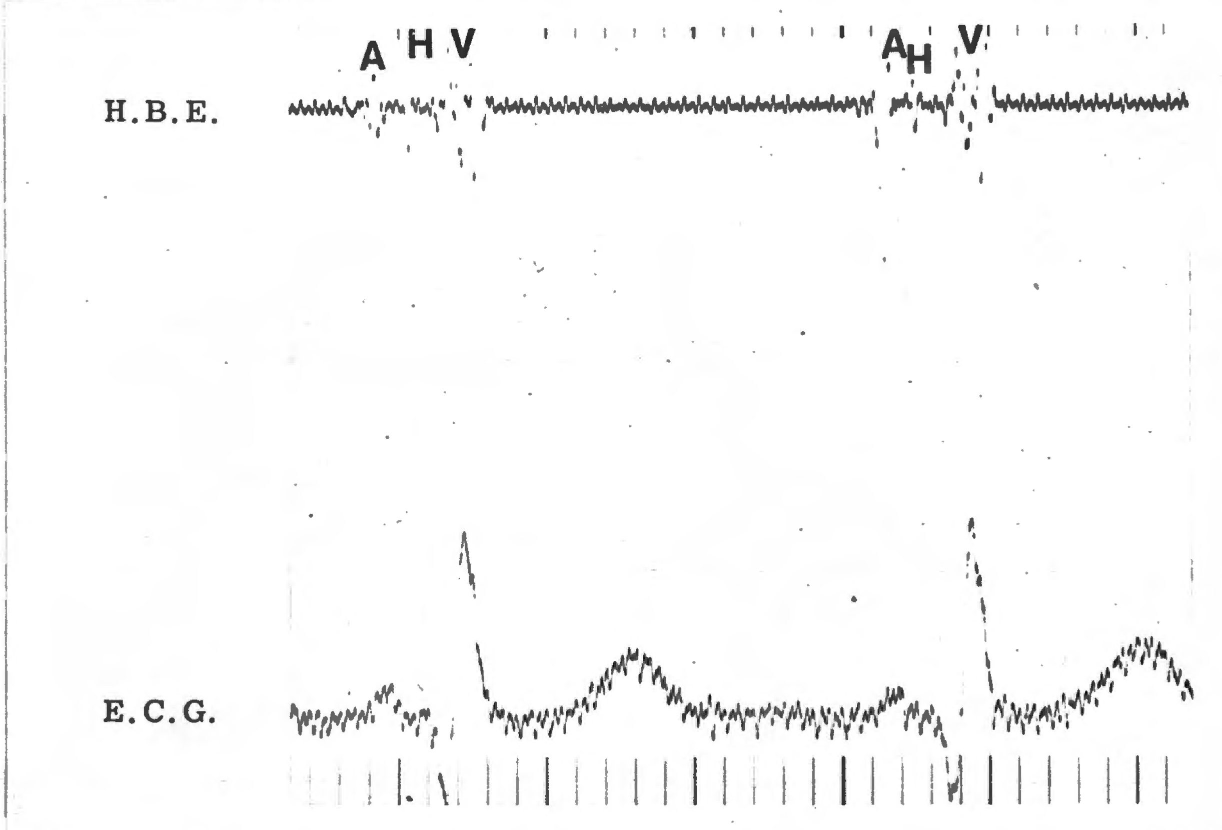


Figure 33 (Case 5) Simultaneous His bundle electrogram (upper panel) and electrocardiogram (lower panel).

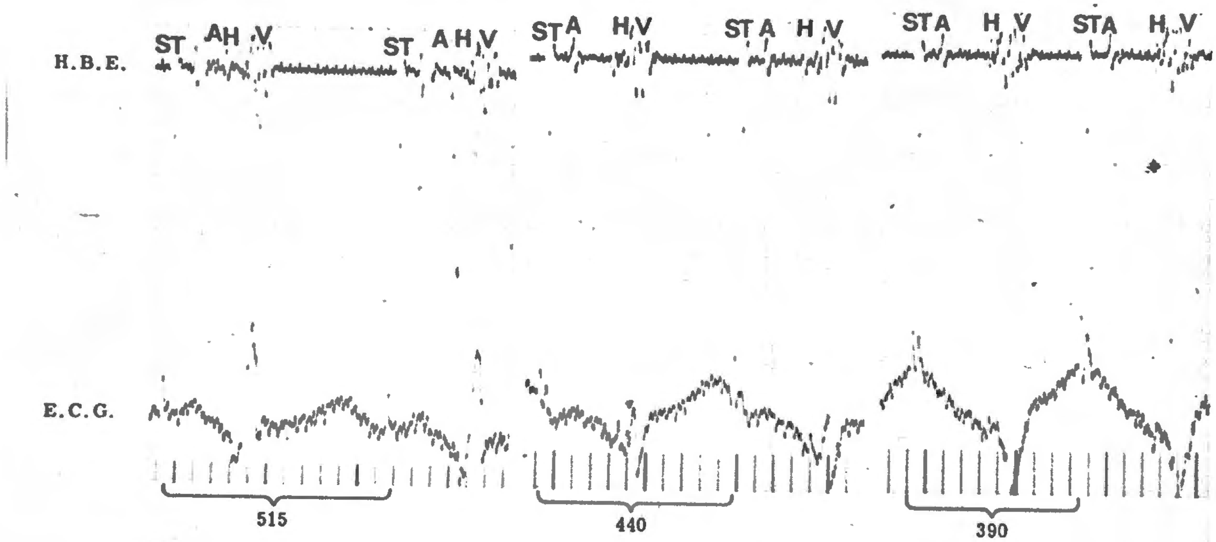


Figure 34 (Case 5) His bundle electrograms and electrocardiograms during progressively faster atrial pacing.

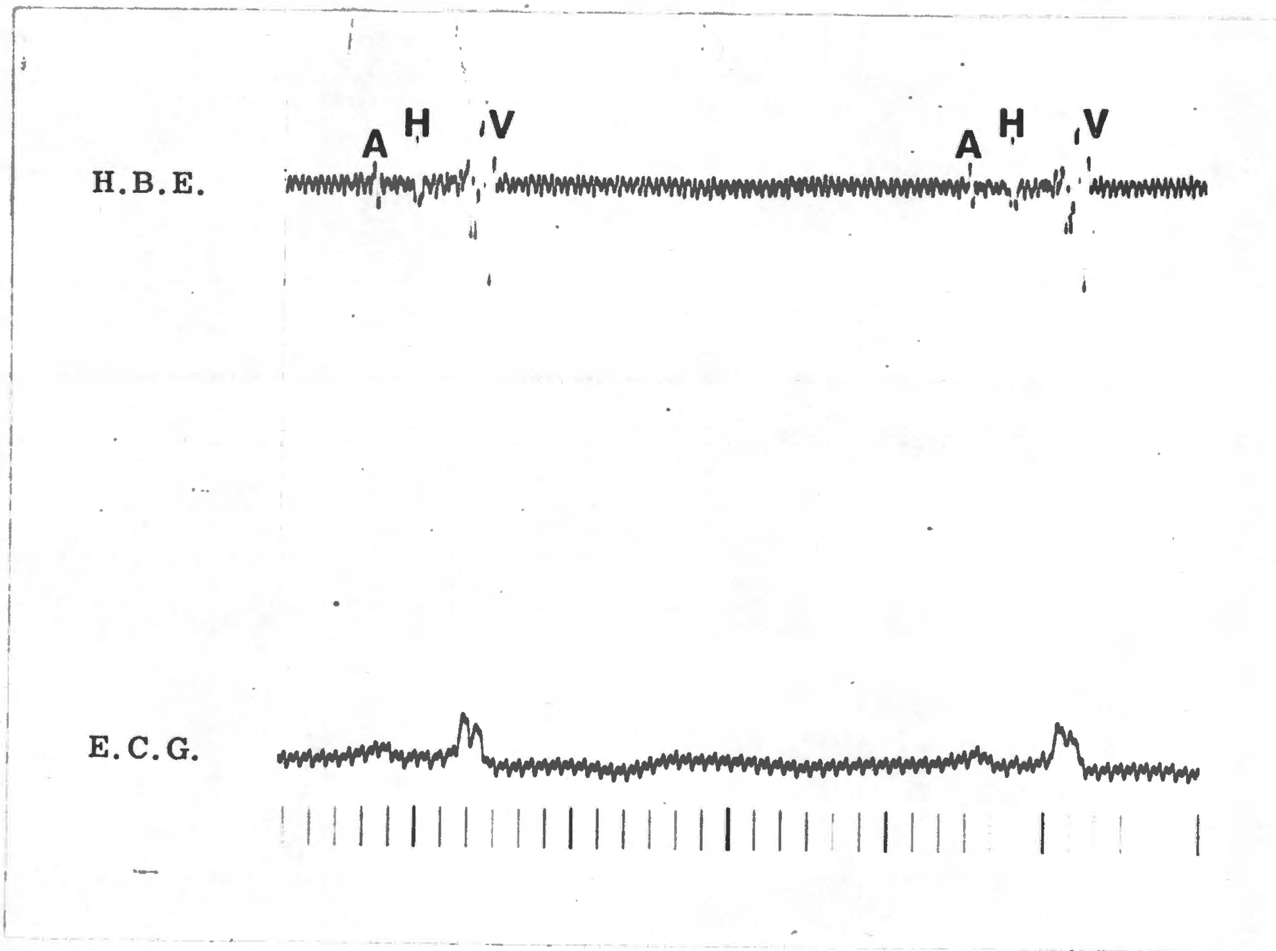


Figure 35 (Case 7) Simultaneous His bundle electrogram and electrocardiogram during sinus rhythm with normal conduction.

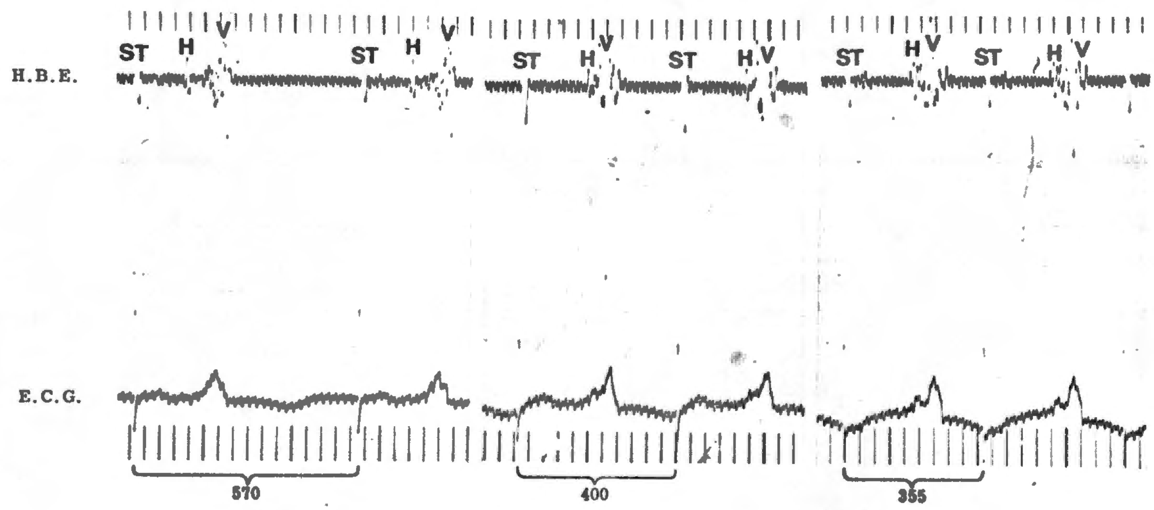


Figure 36 (Case 7) Simultaneous His bundle electrogram and electrocardiogram during right atrial pacing at progressively faster rates.

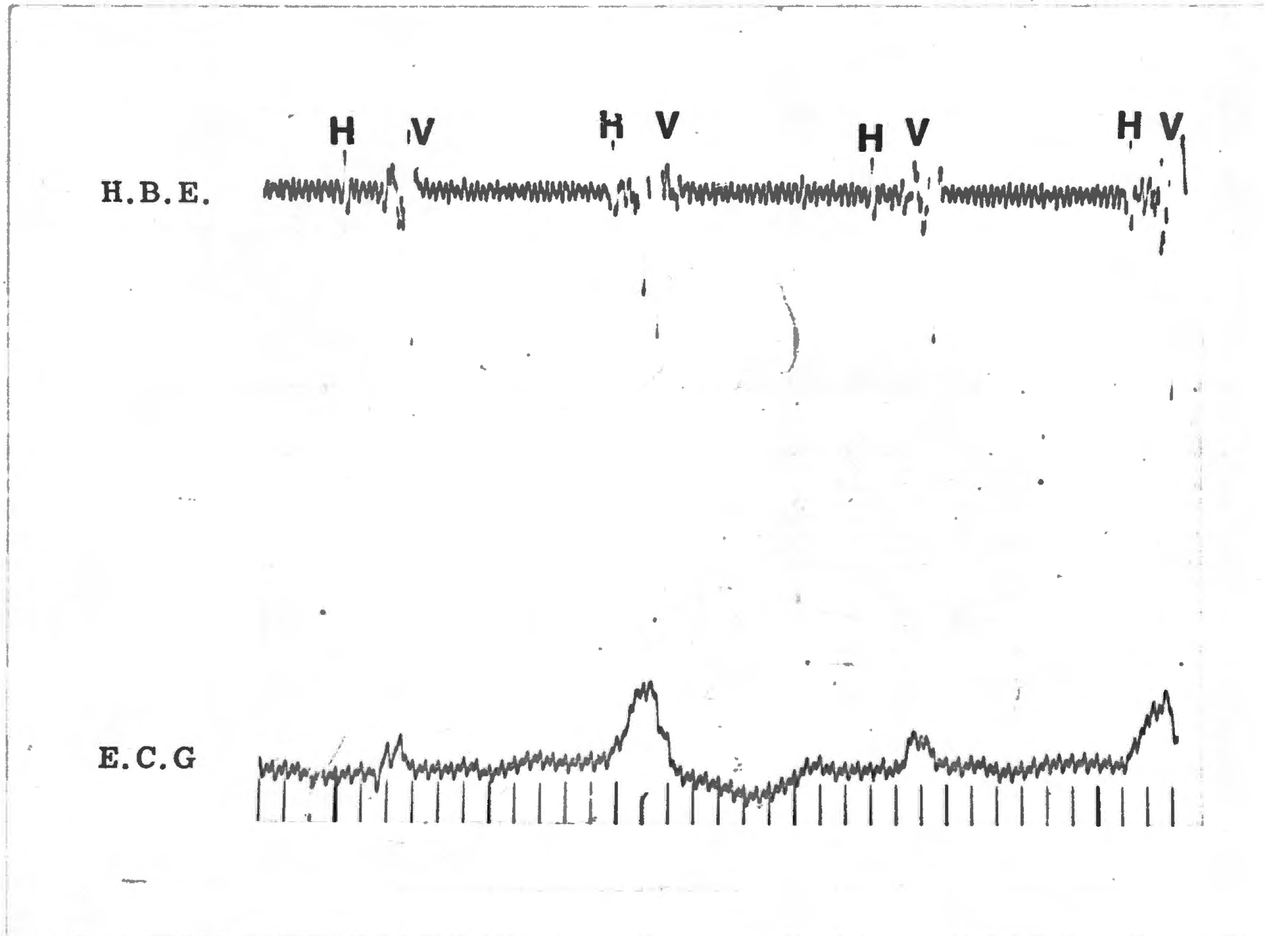


Figure 37 (Case 7) Simultaneous His bundle electrogram and electrocardiogram during alternating normal and Wolff-Parkinson-White conduction.

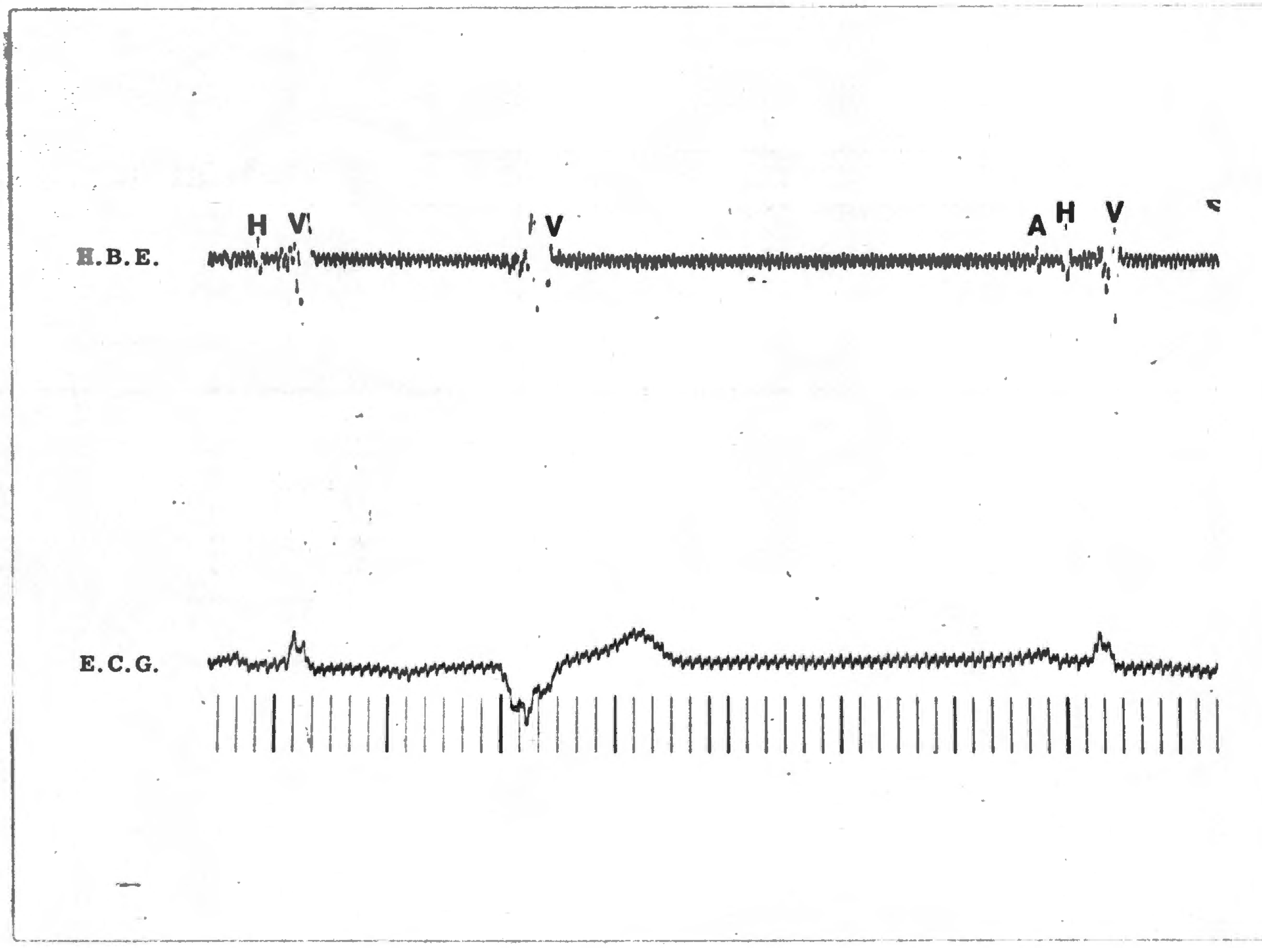


Figure 38 (Case 7) Simultaneous His bundle electrogram and electrocardiogram, showing ventricular extrasystole.

CHAPTER 7

Lown-Ganong-Levine Syndrome

Some twenty years after characterization of the Wolff-Parkinson-White syndrome, Lown et al. (1952) defined a new entity in which the P-R interval is short, but the QRS complex normal; as in the Wolff-Parkinson-White syndrome, there was a tendency to paroxysmal tachycardia. Yet these were not the first workers to postulate that such an entity exists, for Hunter et al. (1940) included three patients with short P-R intervals only with their 19 typical cases of the Wolff-Parkinson-White syndrome. Of these three, one had paroxysmal tachycardia. Although Lown et al. (1952) thought that their cases were caused by an endocrine disturbance, Hunter et al. (1940) felt that they belonged to the same type of disorder as the Wolff-Parkinson-White syndrome.

Two issues arise at once: the definition of the lower limit of normal for the P-R interval; and other possible causes of its shortening. As regards the first, Durrer et al. (1970) and Castellanos et al. (1971b) took 0.12 seconds or less as indicating shortening, though conceding that up to 2% of apparently normal individuals may have P-R intervals of 0.10-0.12 seconds (Scherf and Cohen, 1964); the limit may be less in children (see below). Scherf and Cohen (1964) list a variety of postulated causes, and the most important of these bear examination.

Ectopic pacemakers

In the past, cases with short P-R interval with upright P waves have been labelled as having "coronary nodal rhythm", said to occur when the impulse originates at the tail of the sinoatrial node with subsequent spread to the right and the left and from the back to the front of the atrium (Katz and Pick, 1956; Eyring and Spodick, 1960). This has never been more than a hypothetical concept. It is equally difficult to prove or disprove the existence of atrioventricular nodal (i.e. junctional) rhythm with positive P waves, except with intracardiac electrography, and reports of these disorders have not been corroborated in this way. Without His bundle electrography it is also impossible to distinguish between utilization of an accessory atrioventricular pathway (the posterior internodal tract) and coronary nodal rhythm; and even so, the criteria for the recognition of the latter - if it exists - have not been worked out. A third possibility - a shift of the pacemaker to a different portion of the sinoatrial node - could explain a change in the appearance of the P wave, but not, by itself, a decrease in the P-R interval. That alterations in P wave morphology may occur in the Wolff-Parkinson-White syndrome, without being related to the heart rate or the degree of pre-excitation, was shown in a single case (Sanghvi et al., 1959) and earlier similar features were noted by Hunter et al. (1940), so the fact that the P wave became flatter in one case (Bellet, 1971) would not argue against the Lown-Ganong-Levine syndrome.

Myocardial infarction

The electrocardiograms of fifty cases of myocardial infarction meeting the requirements of the Criteria Committee (1964) were analyzed. In the first place, all patients had a history of central chest pain of at least 30 minutes duration and were admitted to hospital. Only cases who survived for more than two weeks were included, to enable at least two tracings to be examined and compared. None of the patients received digitalis. Only patients who remained in sinus rhythm during this time and did not develop bundle branch block were included. The P-R and QRS intervals were measured on an electrocardiogram recorded on admission as well as one taken 14-17 days later. In each case the site of the infarct is noted. The details appear in Table IX. In no case was the P-R interval shorter than 0.12 seconds, and it was this low in a single case.

The findings in this small series therefore do not support the suggestion that cardiac infarction is an important cause of shortening of the P-R interval. In many of these cases five or more tracings were recorded over a period of 4-5 weeks, and not a single patient with a short P-R interval was encountered. Apart from the data recorded in Table IX, another fifty patients with healed cardiac infarction who attended for routine follow-up had electrocardiograms taken, and in none was the P-R interval less than 0.12 seconds.

<u>Hypertension</u>

The electrocardiograms of fifty patients with hypertension (blood pressure exceeding 180/110 mm.Hg)

Table IX

Cardiac Infarction

	Initial tracing		Subsequent tracing		Site of Infarct
Case	P-R (seconds)	QRS (seconds)	P-R (seconds)	QRS (seconds)	
I.1	0.15	0.08	0.16	0.08	Inferior
I.2	0.16	0.06	0.16	0.06	Inferior
I.3	0.20	0.06	0.20	0.06	Inferior
I.4	0.14	0.08	0.16	0.08	Anterior
I.5	0.16	0.07	0.16	0.07	Anterior
I.6	0.12	0.08	0.12	0.08	Anterior
I.7	0.18	0.06	0.18	0.06	Inferior
I.8	0.15	0.06	0.16	0.06	Anterior
I.9	0.14	0.08	0.14	0.07	Anterior
I.10	0.14	0.06	0.14	0.06	Inferior
I.11	0.16	0.06	0.15	0.07	Anterior
I.12	0.15	0.08	0.16	0.10	Anterior
I.13	0.14	0.10	0.14	0.10	Anterior
I.14	0.16	0.06	0.16	0.06	Inferior
I.15	0.16	0.08	0.16	0.10	Anterior
I.16	0.14	0.08	0.14	0.07	Anterior

Table IX (continued)

Case	Initial tracing P-R (seconds)	Initial tracing QRS (seconds)	Subsequent tracing P-R (seconds)	Subsequent tracing QRS (seconds)	Site of Infarct
I.17	0.14	0.06	0.16	0.06	Inferior
I.18	0.14	0.06	0.14	0.06	Inferior
I.19	0.16	0.08	0.16	0.10	Anterior
I.20	0.18	0.06	0.16	0.06	Inferior
I.21	0.14	0.08	0.16	0.08	Inferior
I.22	0.14	0.08	0.14	0.07	Anterior
I.23	0.16	0.08	0.16	0.08	Anterior
I.24	0.16	0.08	0.16	0.10	Anterior
I.25	0.16	0.10	0.14	0.08	Inferior
I.26	0.16	0.08	0.16	0.08	Inferior
I.27	0.18	0.08	0.20	0.08	Anterior
I.28	0.20	0.10	0.20	0.10	Anterior
I.29	0.18	0.10	0.18	0.10	Anterior
I.30	0.14	0.08	0.14	0.08	Anterior
I.31	0.20	0.08	0.16	1.08	Inferior
I.32	0.18	0.06	0.18	0.06	Inferior
I.33	0.16	0.08	1.16	0.08	Anterior
I.34	0.16	0.10	0.16	0.10	Anterior
I.35	0.14	0.08	0.14	0.08	Inferior

Table IX (continued)

Case	Initial tracing P-R (seconds)	Initial tracing QRS (seconds)	Subsequent tracing P-R (seconds)	Subsequent tracing QRS (seconds)	Site of Infarct
I.36	0.14	0.08	0.14	0.08	Inferior
I.37	0.13	0.06	0.13	0.06	Anterior
I.38	0.16	0.06	0.16	0.08	Anterior
I.39	0.14	0.08	0.18	0.08	Inferior
I.40	0.14	0.08	0.16	0.08	Inferior
I.41	0.16	0.10	0.16	0.10	Anterior
I.42	0.18	0.08	0.20	0.08	Inferior
I.43	0.20	0.10	0.20	0.10	Anterior
I.44	0.15	0.08	0.16	0.08	Anterior
I.45	0.16	0.08	0.16	0.08	Anterior
I.46	0.20	0.10	0.16	0.08	Anterior
I.47	0.16	0.08	0.16	0.08	Anterior
I.48	0.14	0.08	0.14	0.08	Inferior
I.49	I.16	0.08	0.16	0.08	Inferior
I.50	0.20	0.08	0.20	0.10	Anterior

were examined. In each case the tracing was the first in the patient's hospital records. Confirmation was obtained from these records that the patient was not taking any antihypertensive medications at the time or for at least one month beforehand, and only cases showing left ventricular hypertrophy according to the criteria of Pagnoni and Goodwin (1952) were included. No patients were taking digitalis. In all cases sinus rhythm was present with normal intraventricular conduction. The P-R and QRS intervals were measured, and are recorded in Table X. Only one of these patients showed a P-R interval as short as 0.12 seconds.

Thyrotoxicosis

The records of twenty patients with thyrotoxicosis on whom an electrocardiogram had been recorded prior to the commencement of therapy were inspected; cases with atrial fibrillation were excluded. Pertinent data appear in Table XI, from which it will again be seen that in no case was the P-R interval shorter than 0.12 seconds. In only three patients were tracings available once the patient had been rendered euthyroid, and the measure-

Table X

Hypertension

Case	P-R interval (seconds)	QRS complex (seconds)
H.1	0.18	0.08
H.2	0.16	0.06
H.3	0.18	0.07
H.4	0.20	0.08
H.5	0.16	0.10
H.6	0.18	0.08
H.7	0.16	0.08
H.8	0.14	0.06
H.9	0.18	0.06
H.10	0.16	0.06
H.11	0.16	0.06
H.12	0.12	0.08
H.13	0.15	0.06
H.14	0.16	0.08
H.15	0.20	0.10
H.16	0.16	0.08
H.17	0.14	0.06

Table X (continued)

Case	P-R interval (seconds)	QRS complex (seconds)
H.18	0.14	0.08
H.19	0.14	0.06
H.20	0.18	0.06
H.21	0.15	0.08
H.22	0.16	0.08
H.23	0.18	0.08
H.24	0.18	0.06
H.25	0.20	0.06
H.26	0.18	0.08
H.27	0.16	0.06
H.28	0.14	0.08
H.29	0.18	0.08
H.30	0.14	0.08
H.31	0.20	0.06
H.32	0.14	0.06
H.33	0.14	0.08
H.34	0.16	0.08
H.35	0.16	0.06
H.36	0.16	0.06

Table X (continued)

Case	P-R interval (seconds)	QRS complex (seconds)
H.37	0.18	0.06
H.38	0.14	0.06
H.39	0.16	0.06
H.40	0.12	0.08
H.41	0.18	0.08
H.42	0.20	0.06
H.43	0.16	0.06
H.44	0.16	0.10
H.45	0.16	0.08
H.46	0.14	0.08
H.47	0.14	0.06
H.48	0.16	0.06
H.49	0.14	0.08
H.50	0.14	0.06

ments in these cases appear in brackets after the original measurements. This small series again provides no support to the suggestion that a short P-R interval is caused by thyrotoxicosis, though they do tend to be somewhat low. This conforms with the experience at New End Hospital, London, that short P-R intervals are not a feature of their patients with thyrotoxicosis (Cecil Symons, personal communication). Theoretically, increased adrenergic drive in thyrotoxicosis might be expected to accelerate conduction within the atrioventricular node, but this does not appear to be of more than marginal importance.

Lepeschkin (1951) and others (Chung et al., 1965) have noted an apparently high incidence of thyrotoxicosis in the Wolff-Parkinson-White syndrome, and the disappearance of the pre-excitation after restoration of the euthyroid state. This has been attributed to the adrenergic effects seen in hyperthyroidism. If this were to be proved, it is plausible that the Lown-Ganong-Levine syndrome could become manifest in the same way, but this has not apparently been encountered.

Thus unless further evidence is forthcoming

Table XI

Thyrotoxicosis

Case	Heart Rate (beats/minute)	P-R (secs)	QRS (secs)	Protein-bound iodine (u/100 ml.)
T.1	96	0.14	0.06	8.8
T.2	113	0.14	0.08	9.2
T.3	136	0.13	0.06	12.3
T.4	115	0.16	0.06	9.3
T.5	120	0.16	0.08	8.8
T.6	105	0.14(0.14)	0.06	8.1
T.7	124	0.15	0.08	10.9
T.8	295	0.16	0.08	8.2
T.9	100	0.14	0.06	9.3
T.10	110	0.14	0.08	9.5
T.11	120	0.12	0.06	9.8
T.12	116	0.14	0.06	9.5
T.13	96	0.16(0.16)	0.06	9.2
T.14	100	0.16	0.08	11.1
T.15	112	0.14	0.08	12.2
T.16	108	0.14	0.06	11.0
T.17	124	0.12(0.12)	0.07	13.1
T.18	108	0.12	0.06	9.2
T.19	100	0.14	0.07	8.5
T.20	108	0.16	0.08	8.8

(preferably based on measurement of intracardiac conduction times) there appear to be no grounds on which one should reasonably ascribe shortening of the P-R interval to myocardial infarction, hypertension or thyrotoxicosis. Should a significantly short P-R interval be found with patients with these disorders, the likeliest explanation is that they in addition suffer from the Lown-Ganong-Levine syndrome. It was impossible to assess possible P-R shortening in active rheumatic carditis or beri beri heart disease as no cases were available for study.

Taking the criteria of a QRS interval of normal duration (0.10 seconds or less) and configuration, with no delta wave, and a P-R interval of 0.12 seconds or less, 24 adults were identified as having the Lown-Ganong-Levine syndrome. Children and adolescents below the age of 16 were excluded because of the tendency for the P-R interval normally to be short in the young (Scherf and Cohen, 1964), as exemplified by Case 15. This child of 7 showed sinus rhythm, and a heart rate of 80 beats a minute. The P-R interval was 0.10 seconds, and the QRS complexes were normal (Figure 39). Whether this is normal or the Lown-Ganong-Levine syndrome remains to be seen, but he is an example of cases of short P-R interval not further considered herein because of his age. There was no history of tachycardia.

The age in these 24 cases ranged from 17 to 82 years. There were 12 males and 12 females, a similar ratio to the female proportion of 55% reported by Lown et al. (1952), and in keeping with the conclusions of others (e.g. Bellet, 1971) that the male preponderance in the Wolff-Parkinson-White syndrome is not seen with this condition; but the numbers are small, and firm conclusions about this aspect may be unjustified. Among twelve cases of "coronary nodal rhythm", eleven were females (Eyring and Spodick, 1960).

Variability and normalization

An important diagnostic consideration proposed by Lown et al. (1952), that the P-R interval in this syndrome remains fixed, is not borne out by experience. Slight variation has been seen in e.g. Case 16. On one occasion, an electrocardiogram showed sinus rhythm at the rate of 80 beats a minute, and was perfectly normal save for a marginally short P-R interval (0.12

seconds) (Figure 40). On another occasion, a tracing recorded immediately after spontaneous return from atrial flutter to sinus rhythm (heart rate 84 beats a minute) showed the P-R interval to be 0.09 seconds (Figure 41). This electrocardiogram also revealed a slight shift of the mean frontal plane axis of QRS to the left, as compared with Figure 40, S-T depression in leads I, II, aVF and V3-V6, and an inverted T in aVL; these changes all proved transient and were doubtless due to the effects of the arrhythmia. In both Figures 40 and 41, the QRS complexes were 0.09 seconds wide and of normal appearance.

More marked variation in the P-R interval occurred in Case 11, where this ranged from as short as 0.08 seconds to as long as 0.14 seconds. In Figure 42, taken during sinus rhythm (75 beats a minute), the P-R was 0.13 seconds and QRS 0.08 seconds in width and normal in configuration. Similar variability has been noted by Schamroth and Krikler (1967b), and an even more marked degree by Bellet (1971), in whose case the P-R interval varied from 0.08 to 0.16 seconds, with slight change in P wave morphology, but not in the heart rate. A very similar case to this, with sudden change in the P-R from 0.08 to 0.13 seconds, was reported by Eyring and Spodick (1960) in their series of "coronary nodal rhythm".

Normalization, with lengthening of the P-R interval, was of course noted by Hunter et al. (1940) in their original paper linking both types of syndrome with short P-R intervals. The only explanation that seems reasonable is the occurrence of varying degrees of block in the bypass, i.e. the posterior internodal tract, thus allowing the impulse to reach the proximal part of the atrioventricular node in the usual manner postulated by Sherf and James (1969). Presumably the mechanisms discussed in Chapter 3 are to some extent applicable here, though normalization of the Lown-Ganong-Levine syndrome has not received as much attention as in the Wolff-Parkinson-White syndrome: it is certainly a less striking phenomenon.

<u>His bundle electrography</u>

This technique has proved helpful in defining the site of the bypass in the Lown-Ganong-Levine syndrome, though the physiological behaviour of this tract during rapid atrial pacing requires further investigation. Castellanos et al. (1971b) were the first to apply this tool to the study of the Lown-Ganong-Levine syndrome. All three patients had short P-R intervals, normal QRS complexes, and a history of paroxysmal tachycardia. In their first patient, a 32-year-old man with a long history of palpitations, the P-R interval was 115 milliseconds and the QRS complexes 80 milliseconds. Slight slurring of the R waves was noted in leads II, III and aVF, but this was not considered to be due to true delta waves. The electrocardiogram showed left ventricular hypertrophy, although the physical examination was negative. The intracardiac electrograms showed that the interval between low right atrial activation and the bundle of His (LRA-H) was 30 milliseconds (lower limit of normal, 50 milliseconds), and as the H-V interval was within normal limits, these findings represent shortening of the atrioventricular conduction time. Atrial pacing failed to increase the LRA-V interval, even when the heart rate was increased to 230 beats a minute. These findings are consistent with a rapidly-conducting atrioventricular nodal bypass operating in forward (and as shown by the response to ventricular stimulation, retrograde) directions. The only points not explained in their patient are the slurring of the R waves in certain leads, and the electrocardiographic evidence of the left ventricular hypertrophy, which must raise the question of possible association with a cardiomyopathy, as discussed in Chapter 13.

Their second case was a normotensive man who suffered from alcoholism and paroxysmal atrial tachycardia and heart failure. Left ventricular hypertrophy was diagnosed radiologically. He had sinus rhythm with a P-R interval of 120 milliseconds and normal QRS complexes. He too had shortening of atrioventricular conduction time with a LRA-H interval of 35 milliseconds and a normal H-V time of 45 milliseconds. Unlike the first case, atrial pacing at rates of over 160 beats a minute produced the degree of prolongation of atrioventricular nodal conduction anticipated in normal individuals, culminating in the Wenckebach phenomenon. This suggests that he had an atrioventricular nodal bypass which could be blocked by rapid pacing, with resultant conduction down the normal atrioventricular nodal pathways; and in this patient it was also possible to demonstrate retrograde activation up this bypass.

The third patient was a normal 41-year-old woman who had suffered from paroxysmal tachycardia for 15 years. She had a slightly short P-R interval, 115 milliseconds, with normal QRS complexes. In her, too, His bundle electrography during sinus rhythm showed a short LRA-H time of 40 milliseconds, and this again indicated that shortening of the P-R interval was due to a reduction in the time between activation of a low part of the atrium and the bundle of His. Atrial pacing again, as in the second case, produced progressive prolongation of the LRA-H (atrioventricular nodal) conduction time, but only when the cycle length was decreased below 550 milliseconds, i.e. at rates of 109 beats a minute and greater. In the second and third cases in this series the normal anticipated delay through the atrioventricular node only became evident with very short cycles, presumably when the absolute refractory period of the James bundle was reached.

The picture becomes more complex when one considers the three patients diagnosed as having this syndrome, studied by Mandel et al. (1971). All three cases had a short P-R interval, normal QRS and recurrent supraventricular tachycardias. In their case 1, P-R intervals varied between 0.10 and 0.12 seconds; in their cases 2 and 3, the range of P-R intervals was 0.12 to 0.14 seconds. Atrial fibrillation was documented in cases 1 and 3. Unlike Castellanos et al. (1971b) and Smithen and Krikler (1972) they recorded high instead of low right atrial electrograms. In cases 1 and 2 there was a short A-H time at low atrial rates but this increased with atrial pacing; in the third patient the A-H time was within the normal range at an atrial rate of 60 beats a minute. All three patients exhibited shortening of the H-V time, being in the range of 24-28 milliseconds, which is below the lower limit of normal of 35 milliseconds. However the A-H time did not increase with atrial pacing to the same extent as is usually seen in normal subjects, i.e. without the presence of a bypass of the atrioventricular node. This they thought, in two of their patients, to indicate a partial atrioventricular nodal bypass. Whether their patients are typical of the Lown-Ganong-Levine syndrome is arguable, for their concept does not fit with the findings in either Case 16 or in the patients reported by Castellanos et al. (1971b). It may suggest a wider spectrum of conduction disturbances presenting with short P-R intervals and normal QRS complexes, which will require further classification as more of these cases are subjected to His bundle electrography. The shortened H-V time in each case suggests the additional presence of Mahaim fibres; had there been a Kent bundle as well as James fibres one might have anticipated that the latter would influence the expression of the former by producing the Wolff-Parkinson-White syndrome with narrow QRS complexes, as postulated by Coumel et al. (1971a).

His bundle electrography was carried out in Case 15. During sinus rhythm the P-R interval was 120 milliseconds, the P-R interval was reduced to 65 milliseconds, but the H-Q interval was normal at 55 milliseconds. The A-H interval (lower limit of normal, 55 milliseconds) was reduced to 45 milliseconds (Figure 43).

The effects of atrial pacing on the A-H interval are shown in Figure 44 and Table XII; the H-V interval remained unchanged throughout. (The small upright deflection preceding V, especially well seen at 620 milliseconds, may represent activation of the right bundle branch.) There is thus shortening of the time from stimulation of low right atrium to activation of the bundle of His at low cardiac rates, but this lengthens with an increase in the heart rate. The short A-H time is entirely compatible with a bypass of the atrioventricular node. Thus the normal atrioventricular nodal delay was probably not reached until the cycle length was sufficiently short to render the abnormal bypass mechanism refractory. As mentioned above, the physiological behaviour of the James fibres has yet to be fully defined. As they contain conducting tissue they are likely to respond differently to the muscular elements that make up the bundle of Kent. The key finding seems to be shortening of the P-H interval, and this was seen in all 15 cases of the Lown-Ganong-Levine syndrome studied by Coumel et al. (1972). Unlike Mandel et al. (1971), they found no shortening of infranodal conduction; and as in Cases 16 and 17, the P-R interval was often variable.

Table XII

Case 16, His bundle electrogram

Heart rate beats/minute	Cycle length R-R milliseconds	A-H interval milliseconds	H-V interval milliseconds
97	620	50	70
133	450	70	70
154	390	90	70

Possible relationship to the Wolff-Parkinson-White syndrome

It would not be surprising if one occasionally saw evidence of Wolff-Parkinson-White conduction in an individual who basically has a short P-R interval only.

The possible relationship of the Lown-Ganong-Levine and Wolff-Parkinson-White syndromes is illustrated by a patient in whom the P-R interval was consistently short, but in whom on some occasions the QRS complexes were normal, but on other occasions the typical widening and delta wave deformity of the Wolff-Parkinson-White syndrome could be induced (Massumi and Vera, 1971). She was a typical case of the Lown-Ganong-Levine syndrome, with short P-R interval and paroxysmal tachycardia (clearly deducible as supraventricular in type). In her, atrial pacing at 150 beats a minute induced prominent delta waves, the P-delta being shorter than the P-R interval seen in sinus rhythm. Possible explanations for the phenomenon are:-

(a) Constant functioning of a bypass of the atrioventricular node, either the posterior internodal tract or an accelerated pathway within the atrioventri-

cular node, with increased current entering and thus activating a Mahaim tract during pacing (when physiological block is induced in the atrioventricular nodal fibres running down to the bundle of His);
(b) Constant functioning of the posterior internodal tract as far as the bundle of His during sinus rhythm, with activation of the distally destined tracts continuous with them in similar fashion;
(c) The presence of a functioning posterior internodal tract or accelerated intranodal pathway during sinus rhythm, with activation of a bundle of Kent by atrial pacing: i.e. two separate pathways, one consistently active, the other latent. When the posterior internodal tract is active, the bundle of Kent is not, and vice versa. If both were active simultaneously, one would of course expect the QRS to be narrow, albeit with a delta wave, as in Case 12, according to Coumel et al. (1971a).

The clinical and electrophysiological evidence thus links the Wolff-Parkinson-White syndrome closely with the Lown-Ganong-Levine syndrome, albeit with a somewhat different electrocardiographic expression. Basically they both appear to result from a short-circuit bypassing the atrioventricular node; the insertion of the distal end of the bypass into the normal conducting tissue, in the Lown-Ganong-Levine syndrome, determines the normality of the QRS complexes.

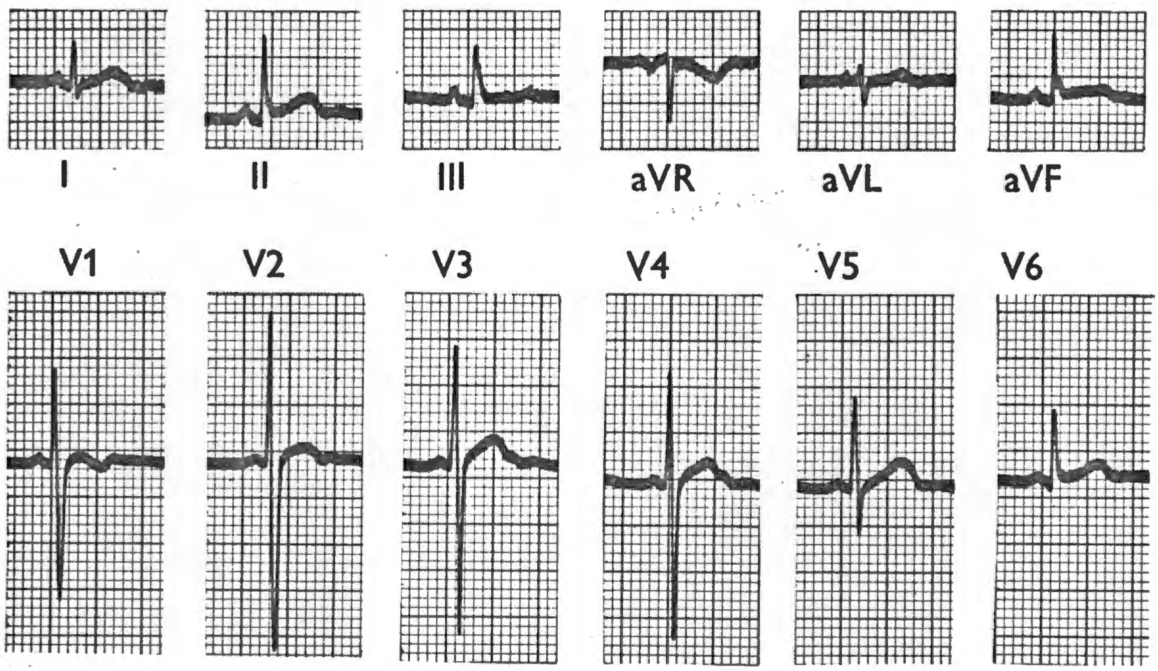


Figure 39 (Case 15) Electrocardiogram, showing short P-R interval.

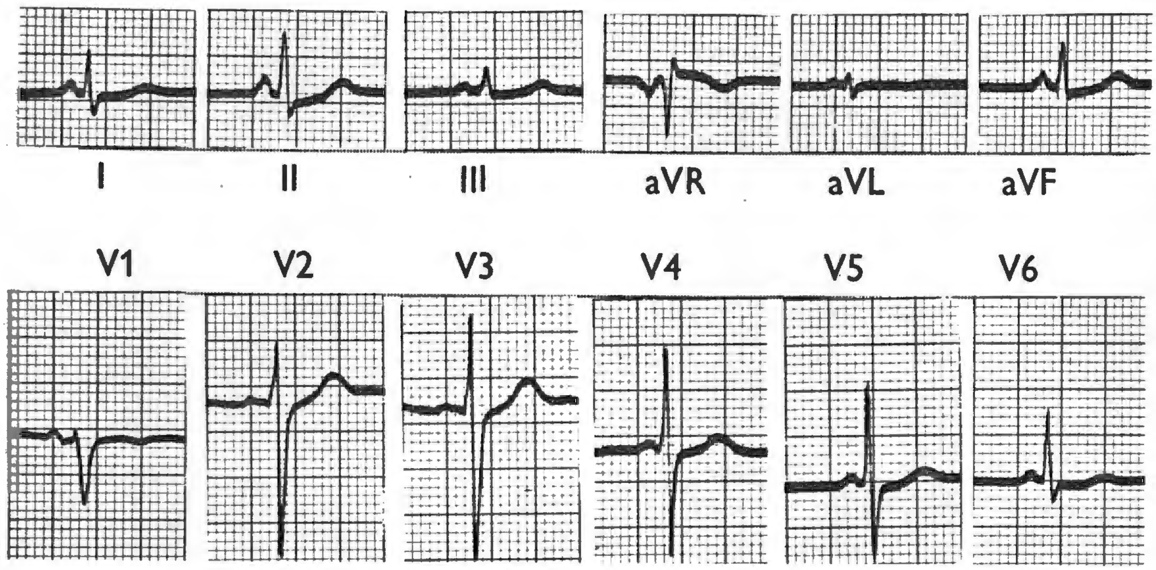


Figure 40 (Case 16) Electrocardiogram showing P-R interval at lower limit of normal (0.12 seconds).

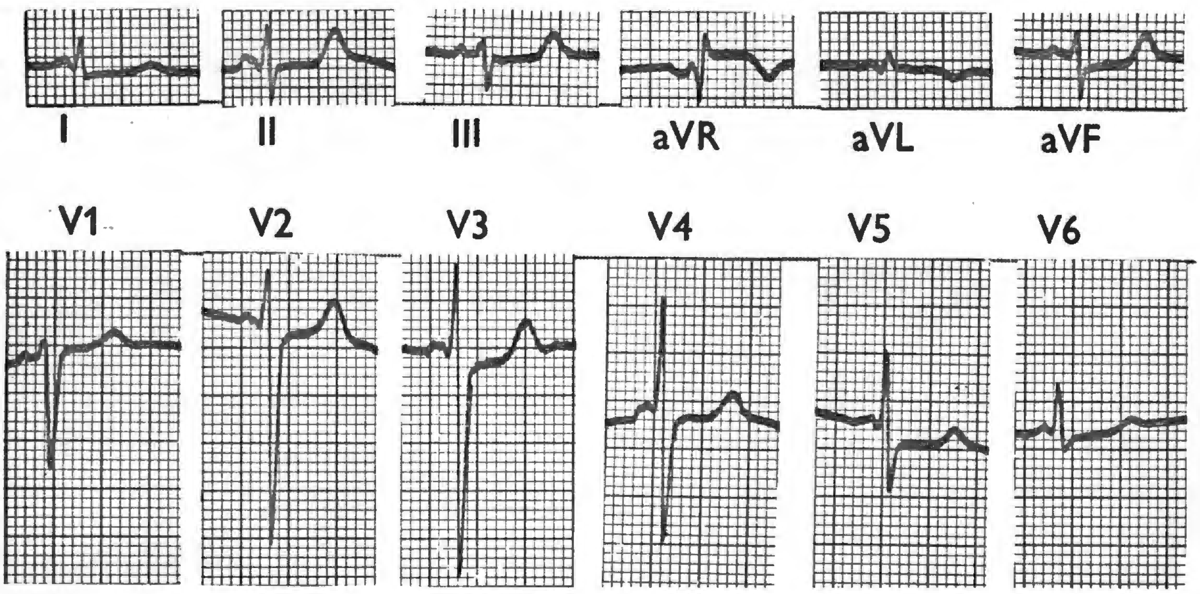


Figure 41 (Case 16) Electrocardiogram recorded immediately after conversion of atrial flutter: P-R 0.08 seconds.

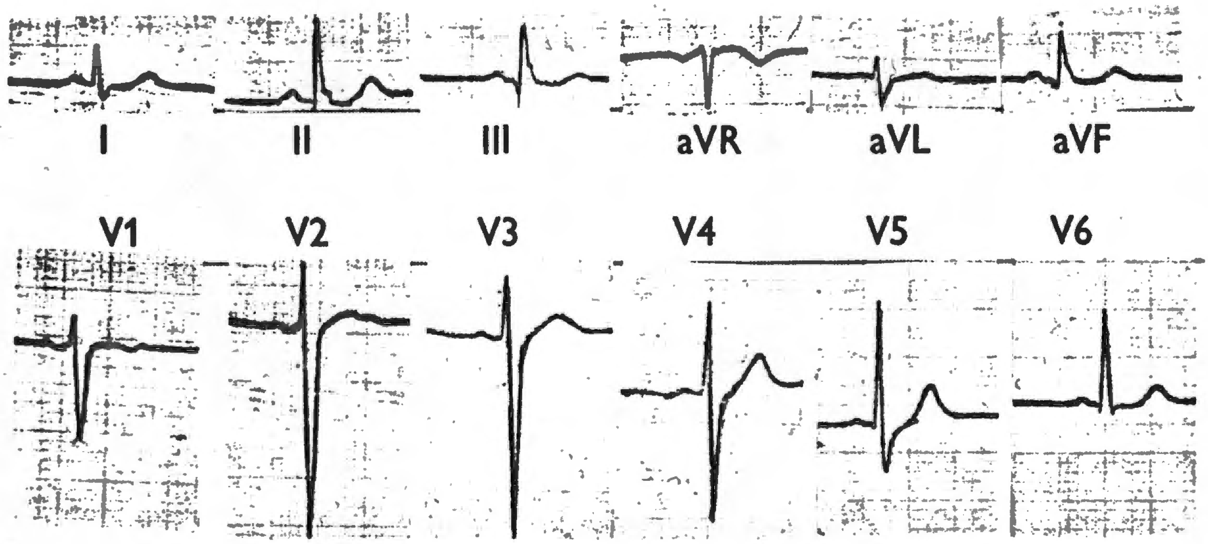


Figure 42 (Case 17) Electrocardiogram, showing sinus rhythm and normal P-R interval on this occasion.

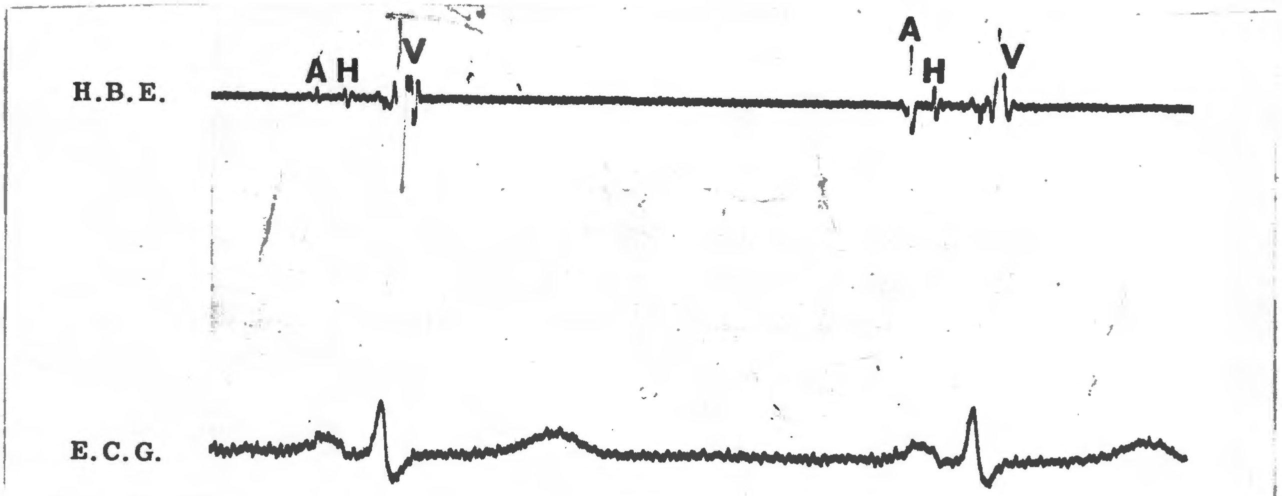


Figure 43 (Case 16) His bundle electrogram taken at rest, showing narrow A-H interval.

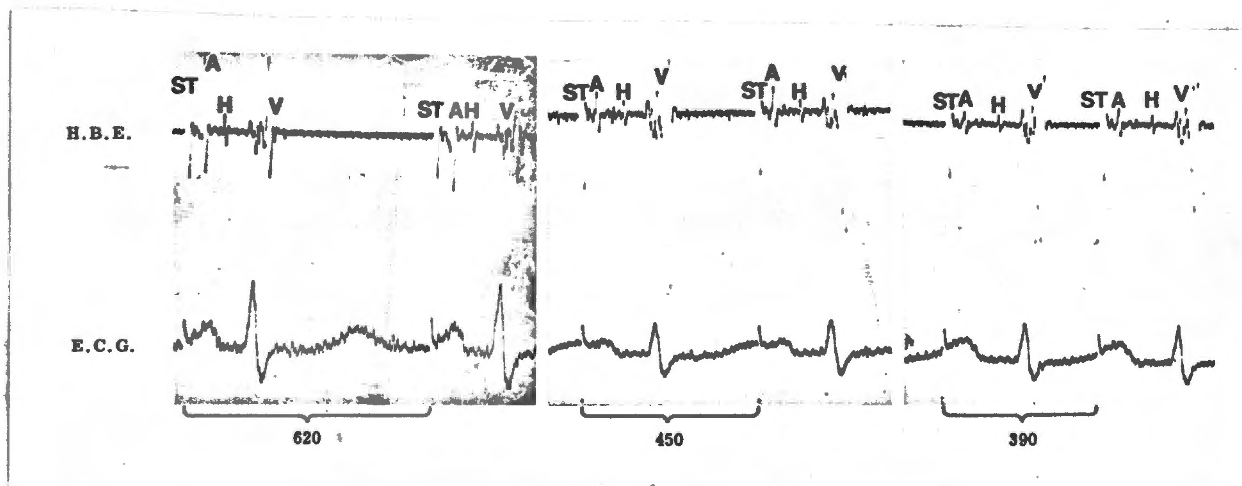


Figure 44 (Case 16) His bundle electrograms during right atrial pacing at increasing speeds; see text and Table XII.

CHAPTER 8

Arrhythmias in the Wolff-Parkinson-White and Related Syndromes

Arrhythmias have been a recognized feature of the Wolff-Parkinson-White syndrome, right from the original report (Wolff et al., 1930) that established the entity. Indeed, the very first case of the syndrome, retrospectively recognized as such, had paroxysmal tachycardia, with such a tracing published Wilson (1915); on the other hand, in his report on paroxysmal tachycardia, Wedd (1921) included a case that we can now recognize as having the Wolff-Parkinson-White syndrome. The incidence and types of arrhythmias, and mechanisms for their production, merit consideration.

According to Bellet (1971), from 40 to 80% of subjects with the Wolff-Parkinson-White syndrome suffer from an associated arrhythmia; 75% in the experience of Wolff (1960). However, one does not know how these cases were collected, and it may be suspected that, as paroxysmal tachycardia is an alarming experience, most sufferers will sooner rather than later have an electrocardiogram, often between attacks, which may well yield the diagnosis of the syndrome. On the other hand, those who are not troubled, may well escape detection, e.g. Case 3, in whom it was only the incidental recording of an electrocardiogram prior to an operation that led to the diagnosis being made. It was on the basis of non-specific left mammary pain, that Case 7 had an electrocardiogram that showed the Wolff-Parkinson-White syndrome (Figure 9), even though a wrong diagnosis was made at that time. It was somewhat different with Case 5; an abnormal-looking electrocardiogram was recorded, but not identified correctly, when he had an episode of paroxysmal tachycardia when young; only later were the appearances recognized. It is instructive in this particular case to think that he first developed paroxysmal tachycardia in 1917, before the syndrome was characterized but after the report by Wilson (1915); an electrocardiogram was recorded a few years later and recognized to be "abnormal".

An understanding of the arrhythmias and of the mechanisms involved depends upon knowledge of the broad principles that can be deduced from the functioning of the anatomical pathways already considered. The usual state of affairs in the Wolff-Parkinson-White syndrome during sinus rhythm is indicated in Figure 1. The refractory period of the normal pathway is shorter than that of the anomalous pathway, so that conduction down the anomalous pathway proceeds more rapidly than it does down the normal tract. If for any reason the anomalous pathway should become refractory to anterograde conduction down it, as shown in Figure 45, panel 2, conduction may now take place anterogradely down the normal pathway instead. Factors which might induce such a state of affairs could include an appropriately timed supraventricular extrasystole, i.e. when the anomalous pathway is unable to conduct in a forward direction, but when the normal pathway can: the appearance of the Wolff-Parkinson-White syndrome will be lost (Figure 22).

How may this mechanism lead to paroxysmal tachycardia? It was De Boer (1926) who originally suggested that paroxysmal supraventricular tachycardia might be due to a circus movement between atria and ventricles in which the impulse returned from the ventricles and fired off the atria again. Indeed, it is now believed that many cases of paroxysmal supraventricular tachycardia, not due to the Wolff-

Parkinson-White syndrome, occur on this basis (Goldreyer and Damato, 1971). When it was suggested that the appearances of the electrocardiogram in the Wolff-Parkinson-White syndrome were due to conduction anterogradely down the bundle of Kent (Wolferth and Wood, 1933), it was at the same time postulated that retrograde conduction up this bundle could initiate a circus movement in reverse that would be responsible for the establishment of paroxysmal tachycardia.

In the normal course of events in the Wolff-Parkinson-White syndrome, the supraventricular impulse travels more rapidly down the anomalous pathway than down the atrioventricular node. However, the refractory period of the anomalous pathway is longer than that of the atrioventricular node. When the heart beats relatively slowly, this discrepancy in the refractory period in the two pathways (i.e. the interval between positions 1 and 2 of Figure 46) is unimportant: the subsequent impulse (impulse 2) will find both pathways responsive. However, with relatively fast rates, the supraventricular impulse may find the normal pathway responsive and the anomalous pathway refractory, as shown by position 3. Under these circumstances anterograde conduction down the anomalous pathway is blocked and the sinus impulse travels anterogradely through the normal pathway only. This same impulse can, however, return retrogradely through the anomalous pathway, as in diagram 2 of Figure 45 - unless it is still refractory as in Case 12 (Figure 22). When the returning impulse reaches the atria prematurely, it may find the atrioventricular node again conductive, and it can then once more pass anterogradely down it to activate the ventricles. This phenomenon may be repeated, in which case one will see a tachycardia. This reciprocating tachycardia, characteristic of the Wolff-Parkinson-White syndrome, is thus due to a circus movement between the anomalous and the normal atrioventricular pathways: retrogradely up the anomalous, and anterogradely down the normal. Therefore the pre-existing appearances of the Wolff-Parkinson-White syndrome, during sinus rhythm, are abolished, and no abnormal QRS complexes will be seen.

When Case 7 presented with paroxysmal tachycardia (Figure 47), the heart rate was usually 200 beats a minute, and the QRS complexes were narrow (0.06 seconds); ST depression or T inversion were consistent features, and the QRS morphology was quite different from that seen during sinus rhythm with anomalous conduction, whether overt (Figure 9) or partially normalized (Figure 10). There is no evidence of atrial depolarization (Figure 45, panel 2).

In Case 11, the electrocardiogram showed the appearances evident in Figure 48. Only limb leads had been recorded, and these showed a regular tachycardia at the rate of 200 beats a minute. The QRS intervals were 0.06 seconds in width, and were followed by P' waves at an R-P' interval of 0.10 seconds. The P'-R interval was 0.18 seconds. The P' waves were inverted in leads I and aVL and upright in leads II, III, aVR and aVF. The absence of the chest leads makes it difficult to identify which atrium is first depolarized with great confidence, and the right axis deviation of the P wave does not conform with the criteria for left atrial rhythm laid down by Mirowski (1967). However, depolarization of the atrial chamber from the distal and left aspect would be expected to produce a P wave axis like this, and is perfectly in keeping with retrograde conduction up a left-sided anomalous pathway, in this case of type A Wolff-Parkinson-White syndrome (Figure 25). The evidence of atrial depolarization is unusual and is exemplified in Figure 45, panel 3.

As has been pointed out by Durrer et al. (1967) and Wellens et al. (1971a and b) the production of extrasystoles at the appropriate time in the cardiac cycle, whether on the right side of the heart or the left, can initiate such reciprocating tachycardias in the Wolff-Parkinson-White syndrome. Right-sided extrasystoles are much more effective in inducing arrhythmias in patients with right-sided bypasses, i.e. the Wolff-Parkinson-White syndrome type B; left-sided extrasystoles are more effective with a left-sided bypass, i.e. Wolff-Parkinson-White syndrome type A.

This tachycardia can be started by an atrial extrasystole at a time when the anomalous pathway is refractory to anterograde conduction, but the normal pathway is responsive; or a suitably timed ventricular extrasystole may find the anomalous pathway responsive to retrograde conduction, but the normal pathways refractory (A and V in Figure 49). Furthermore, these workers have shown that the production of an extrasystole at the appropriate time during the tachycardia can interrupt this circus movement and enable the sinoatrial node to regain its function as the primary cardiac pacemaker, with restoration of sinus rhythm and Wolff-Parkinson-White conduction.

The production of a paroxysmal arrhythmia in this way was observed in Case 5. After right ventricular stimulation, the patient developed supraventricular tachycardia at the rate of 180 beats a minute (Figure 50). In Figure 51, in the simultaneous His bundle electrogram, a His potential is clearly evident preceding each QRS complex, now at a normal H-Q interval of 40 milliseconds; no retrograde His potentials are visible. Although neither the beginning nor the end of the tachycardia was recorded, these appearances are consistent with a re-entry mechanism with anterograde conduction by the bundle of His and retrograde conduction via an anatomical tract bypassing the bundle of His, as shown in the cular extrasystoles interrupted the circuit by reaching but not passing retrogradely through the atrioventricular node but interrupting the circuit. Durrer et al. (1967) and Massumi et al. (1970) have also previously shown that reciprocating tachycardias in the Wolff-Parkinson-White syndrome can be terminated by atrial and ventricular stimulation in a similar fashion.

In their first case (Castillo and Castellanos, 1970) reciprocating tachycardia was established 160 milliseconds after an induced premature atrial beat; a His bundle deflection occurred at that time and this preceded the onset of a different QRS complex by 50milliseconds, a normal value for conduction anterogradely down the bundle of His. The marked left axis deviation of the QRS complexes is in keeping with the possible presence of left anterior hemiblock. This arrhythmia was considered to have resulted either from a circus movement involving two anatomically separate communications, the bundles of His and Kent, or from functional intranodal dissociation (Moe and Mendez, 1966). This patient also showed a brief run of atrial flutter which converted rapidly to atrial fibrillation. During the atrial fibrillation, conduction appeared to occur anterogradely mainly through the bundle of His, again showing left axis deviation. It was thought that an atrial extrasystole might have triggered atrial fibrillation when falling in the vulnerable period of the atria (Bennett and Pentecost, 1970).

In the second patient, the occurrence of an atrial extrasystole during the period of atrial vulnerability also set off atrial flutter, with stimulation of the ventricles through the bundle of Kent to a greater degree than the bundle of His.

In the third patient, a reciprocating tachycardia was initiated by mechanical stimulation of the right ventricle resulting in extrasystoles; these were followed by retrograde P' waves which were in turn followed by His deflections at a P'-H interval of 280 milliseconds. During this paroxysmal reciprocating arrhythmia the anterograde conduction was further evidenced by narrow, normal, QRS complexes, with normal P-R intervals, similar to those that had occurred spontaneously in this patient.

As indicated in the preceding section, it has been shown that arrhythmias can be produced following the induction of extrasystoles - atrial or ventricular - by means of intracardiac stimulation of the right-sided cardiac chambers, when the bypass itself is right-sided (i.e. the conduction shows the type B pattern of the Wolff-Parkinson-White syndrome (Durrer et al., 1967)). Left-sided endocardial stimulation is technically more difficult to achieve, but it is possible, and the corresponding state of affairs has been demonstrated by the same group of workers (Wellens et al., 1971a): arrhythmias were produced following the induction of left atrial or ventricular extrasystoles in this way, in cases where the bypass was left-sided (type A Wolff-Parkinson-White conduction). Having type A conduction, Case 5 has a left-sided bypass; yet right-sided stimulation led to the arrhythmia; and no easy explanation for this comes to mind, save that the impulse must have spread across to the left at the appropriate time in the cardiac cycle. The extrasystoles recorded on ordinary electrocardiograms in this patient had been scanty and were too few for precise localization.

According to the criteria of Rosenbaum (1969) the extrasystoles seen in Figure 52 can be of left ventricular origin; and if the patterns in Figures 52a and b (albeit occurring on different occasions, and with and without pre-excitation in the sinoatrial beats) are of the same import, this can be substantiated. These left-sided ventricular extrasystoles could thus have gained access to the left-sided bypass in this patient, and led to paroxysmal tachycardia.

A similar situation is seen in Case 7. In Figure 29, the pattern of the extrasystoles shows them to be ventricular in type, with left axis deviation and tall R waves in right precordial leads, in keeping with an origin from the posterobasal region of the left ventricle (Rosenbaum, 1969). In some leads it is possible to see retrograde P' waves deforming the commencement of the ST segment, and this is most clearly evident in leads II, V1 and V2. Well-marked Q waves are present in the extrasystoles in leads I, II, aVL and V4-6. The extrasystoles in this case illustrate another point made by Wolff (1954); he said that the P-R and R-P' intervals should be the same, thus indicating the possibility for anterograde or retrograde use of the anomalous pathway. This applies, although not precisely here; the P-R interval was 0.11 seconds and the R-P' 0.12 seconds; it is very possible that this slight discrepancy is due to the fact that one could not accurately delineate the start of the P' from the preceding QRS complex.

At this stage one must question whether conduction in a bypass must needs always take the same time in either direction, as proposed by Wolff (1954), for in Case 11 the P'-R and R-P' intervals were different (Figure 47); but the P-R interval in sinus rhythm (Figure 25) was close to the R-P' during paroxysmal tachycardia (Figure 48). The problem of multiple pathways and their role needs further evaluation (Friedberg and Schamroth, 1972).

The mere existence of these extrasystoles does not mean that the tachycardias arose on their account. However, not too much must be made of the localization of extrasystoles that are seen, but that do not lead to paroxysmal tachycardias, for these might not be the extrasystoles that generated the arrhythmias.

It is nevertheless an interesting speculation that certain extrasystoles might be more hazardous in a patient with the Wolff-Parkinson-White syndrome, depending both on the ventricle in which they arise and on the location of the bypass.

This raises the very important question: may patients with the Wolff-Parkinson-White syndrome fail to survive purely because of the arrhythmias? Life assurance statistics (Wolff, 1959) indicate a mortality of roughly 2½ times that to be expected in normal subjects, among those who suffer from this syndrome. This presumably only applies to those who have been recognized as suffering from it, which is likely to include a high percentage of cases who already have arrhythmias, and one must seriously question whether the outlook is dismal for all cases, and whether the isolated individual, found to have the appearances on an electrocardiogram recorded routinely, is especially at risk. Thus Okel (1968) indicated no excess mortality in such cases. The one significant difference between Cases 5, 7 and 12 (on the one hand) and Case 3 (on the other), is that the three former cases, prone to paroxysmal tachyarrhythmias, had extrasystoles, whereas the latter did not. But there is more to it than this. In those with arrhythmias, these either first occurred or became much more frequent and worse after the age of 60, and there is some evidence on the tracings during normalization, and in the pattern of his extrasystoles, to believe that Case 7 has suffered from a cardiac infarct. It is not possible to state whether this occurred as a consequence of poor coronary flow during an attack of paroxysmal tachycardia; this is certainly possible, for marked ST depression was clearly evident on some occasions, and he usually suffered pain with these attacks. On the other hand, a cardiac infarct that left behind an ischaemic area from which ventricular extrasystoles could arise, easily provides the focus from which such extrasystoles could be generated and also enter the anomalous pathway retrogradely, at times when the normal pathway is refractory and the anomalous pathway is receptive and able to conduct stimuli. The steady increase in the frequency of extrasystoles in normal individuals as age advances (Simonson, 1972) is usually unimportant clinically. If however, a situation exists where these can initiate arrhythmias by entering reciprocal pathways, they may be hazardous. During intracardiac electrography, no arrhythmia could be initiated by cardiac stimulation in Case 7, and this might be explained because (having type A Wolff-Parkinson-White conduction) his bypass was left sided and not entered. In Case 1, it was hoped that atrial or ventricular stimulation might more easily produce an arrhythmia in view of the fact that he had type B Wolff-Parkinson-White conduction, and that an extrasystole produced on the right side of the heart might more easily enter any pathway capable of reciprocal conduction; but it proved impossible to induce extrasystoles or initiate an arrhythmia. Thus not all patients are responsive to appropriate stimulation; this may explain the freedom from arrhythmias in some. Not all arrhythmias in the Wolff-Parkinson-White syndrome represent paroxysmal supraventricular tachycardia, and experience in the 74 cases analysed (Table XIII) shows that atrial fibrillation occurs sufficiently often to be an important complication. The way in which this is induced is discussed in Chapter 9, and further discussion of mechanism will be deferred until then.

As will be seen from Table XIII, 25 of the 74 cases had an arrhythmia (with probable paroxysmal arrhythmia in another 5, to make a total of 30): less than the incidence quoted by Wolff (1960) (see above), but above the 12% in the 187 healthy airmen with the Wolff-Parkinson-White syndrome discovered by Averill et al. (1960).

In the Lown-Ganong-Levine syndrome, basically the same mechanism is operative, save that the pathway utilized is anatomically of course slightly different (see Chapters 2 and 7). The situation, with the pathway either within or very close to the atrioventricular node is shown in Figure 53. During sinus rhythm, there is more rapid transmission through the anomalous pathway than the normal one; during paroxysmal tachycardia, or with atrial fibrillation, the normal pathway may be utilized, but as they are close together, it is of less importance which pathway is used anterogradely. A circus movement, analogous to that in the Wolff-Parkinson-White syndrome, is set up (Figure 53, panel 5); the QRS complexes, which were

Table XIII

Arrhythmias in The Wolff-Parkinson-White syndrome

Arrhythmia	Number of Cases
Supraventricular tachycardia	17 *
Atrial flutter	1
Atrial fibrillation	8 *
History suggestive of arrhythmia but no confirmation	5

* Includes one patient with both arrhythmias on different occasions.

Table XIV

Arrhythmias in Lown-Ganong-Levine syndrome

Arrhythmia	Number of Cases
Supraventricular tachycardia	10
Atrial flutter	1
Atrial fibrillation	2
History suggestive of arrhythmia but no confirmation	1

narrow to start with, will not change their appearance.

The incidence of arrhythmias in the 24 cases of the Lown-Ganong-Levine syndrome is shown in Table XIV. It will be seen at once that the incidence (57%) is higher than the 40% among the 74 cases of the Wolff-Parkinson-White syndrome, but the relatively small number of cases may have led to chance emphasis on the former syndrome. What is probably of greater importance is that the electrocardiographic features of the Wolff-Parkinson-White syndrome are much more likely to be noticed by the inexperienced observer than an isolated short P-R interval, for the latter is not a disorder that the electrocardiographic reporter is usually taught to seek. In a series of 15 cases of the Lown-Ganong-Levine syndrome, intractable atrial flutter or fibrillation was found to be the commonest arrhythmia (Coumel et al., 1972). The mechanism of atrial fibrillation in the Lown-Ganong-Levine syndrome - as well as in the Wolff-Parkinson-White syndrome - will be discussed in Chapter 9; but an example of each of the other arrhythmias will be presented:-

Paroxysmal supraventricular tachycardia

A representative tracing taken during paroxysmal supraventricular tachycardia (Case 17) is shown in Figure 54, where the heart rate is 200 beats a minute, and the P'-R interval, 0.18 seconds, is longer than during sinus rhythm (Figure 42). The basic shape and the duration of the QRS complexes was unchanged during the paroxysmal tachycardia, though the S waves are slightly more prominent in e.g. leads I and V6, and the upstroke of S in V1 is slightly slurred. It is feasible that these changes indicate a minor degree of aberration of intraventricular conduction, affecting the right bundle branch. The P'-R interval during the paroxysmal tachycardia was equal to the R-P' interval. In V5 and V6 the R waves alternate in height, but in V4 this is inconsistent; it is plausible that the normal and anomalous pathways are being used anterogradely in turn.

An analysis of the tracings showed that the P' waves are of a different configuration from those seen during sinus rhythm and are predominently upright in leads I and aVL, and inverted in II, III and aVF. They were also upright in V1, V2, V3 and V4, probably inverted in V5, and clearly inverted in V6. This suggests that the atrial chamber is being depolarized from its inferior part, but whether left (Mirowski, 1967) or right is impossible to say; nor was there any change in relation to the alteration of the R waves. Once again the closeness of the anomalous pathway to the atrioventricular node renders assessment impossible, using the surface electrocardiogram.

The onset of paroxysmal tachycardia in this case is shown in Figure 55. During sinus rhythm, when the basic P-R interval was 0.12 seconds, an atrial extrasystole can be seen(V1) with an rsR' pattern of functional right bundle branch block (Sandler and Marriott, 1965). The P'-R interval of this beat was slightly longer, 0.15 seconds. In V3 an extrasystole of similar configuration can be seen following the T wave of the first sinus beat, but no preceding P wave can clearly be seen although the extrasystole is followed by an inverted P' complex, at a rather long R-P' interval of 0.26 seconds. The third complex visible is a sinus beat and it too is followed by a P' at an identical R-P' interval; then follows paroxysmal supraventricular tachycardia at a rate of 200 beats a minute. The reciprocal mechanism is here clearly evident.

In the Lown-Ganong-Levine syndrome, Castellanos et al. (1971b) were able to induce reciprocating tachycardia by atrial stimulation in only one of their cases, and this arrhythmia stopped spontaneously when an impulse was blocked within the atrioventricular node during its anterograde passage. Here the findings were compatible with either an atrioventricular nodal bypass operating in both directions or a single, functionally dissociated, anatomical atrioventricular nodal pathway, e.g. the posterior internodal tract.

Atrial flutter

All three observed episodes of palpitations in Case 16 were shown to be atrial flutter (Figure 56), but spontaneous onset or cessation was not recorded. Although a reciprocal mechanism could initiate the atrial flutter, i.e. retrograde conduction into the atria could set off the arrhythmia, a circus movement involving the normal and anomalous pathways is not responsible for its maintenance, as the atrial flutter is accompanied by 2:1 atrioventricular response. As will be seen in Figure 56, the ventricular rate was 160 beats a minute, and the atria fluttered at double this speed. These comments are not meant to contradict the possibility that an atrial circus movement is responsible for atrial flutter. With anterograde block shown by the ventricular response, an atrioventricular circus movement would thereby be blocked.

The initiation of atrial fibrillation in patients with pre-excitation - and the response of the ventricles - will be discussed in Chapter 9.

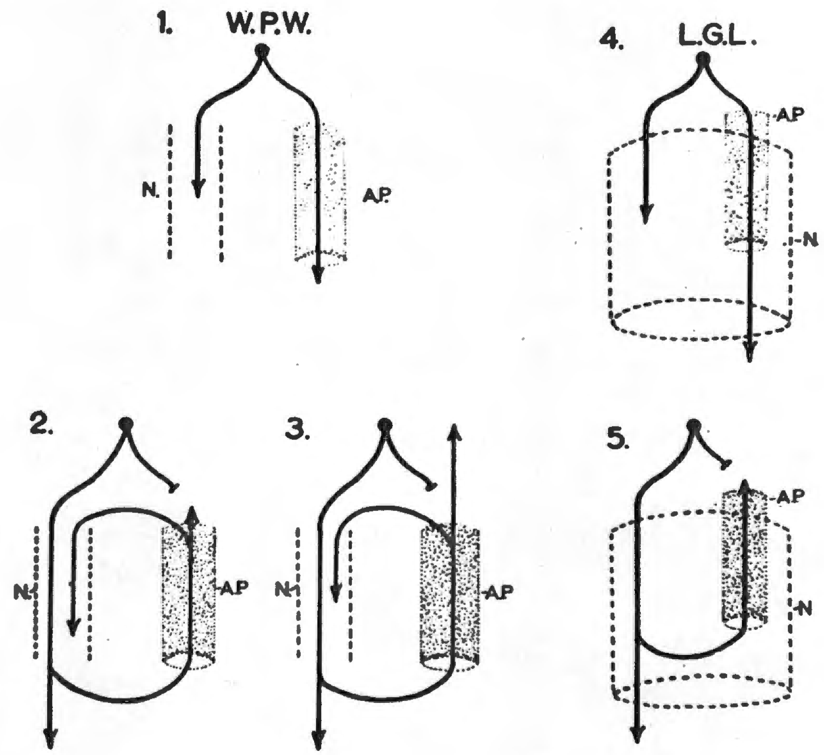


Figure 45 Diagram to show conduction pathways in Wolff-Parkinson-White syndrome (1), Lown-Ganong-Levine syndrome (4), paroxysmal tachycardia complicating Wolff-Parkinson-White syndrome (2), reciprocating tachycardia (3) and paroxysmal tachycardia complicating Lown-Ganong-

dotted line in the ladder diagram at the bottom of Figure 51. This has the features of supraventricular tachycardia with a narrow QRS complex, the appearances (as seen in Figure 50) differing from those during the usual pattern of pre-excitation encountered in this patient (Figure 8), there being more resemblance to that seen in a tracing recorded when he exhibited a pattern of normalized conduction (Figure 7).

During a study by Castillo and Castellanos (1970) the mode of termination of the arrhythmias was investigated. In the first two patients, the reciprocating tachycardias were stopped by carotid sinus pressure, which produced progressive lengthening of the P'-R and P'-H intervals until a P' failed to reach the bundle of His. This is very similar to the demonstration by Goldreyer and Bigger (1970) of the basically similar mechanism in patients with presumed re-entry tachycardia not due to the Wolff-Parkinson-White syndrome. Atrial capture could be achieved by early atrial extrasystoles, preventing the returning P' wave from capturing the ventricles again. In the third case mechanically induced ventri-

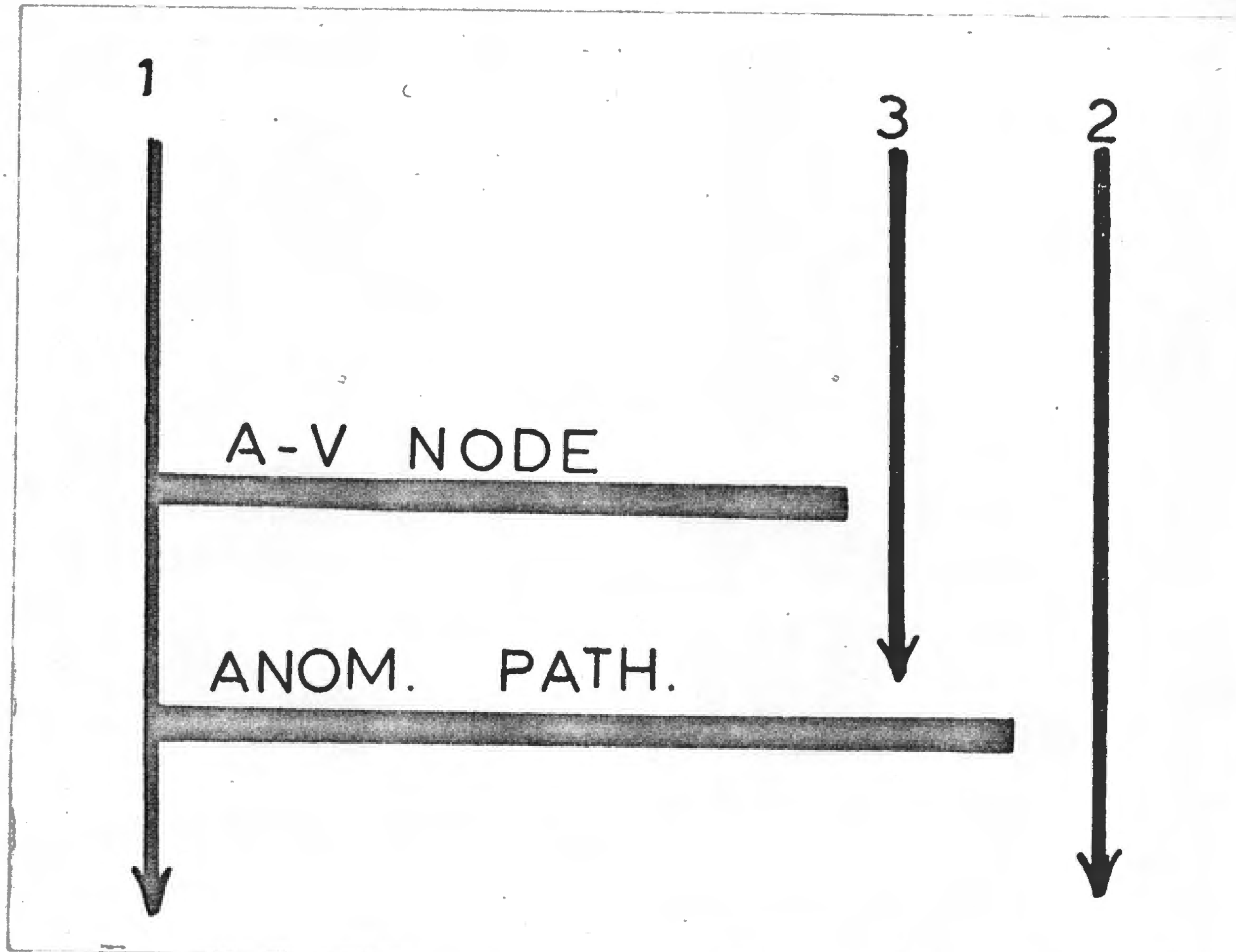


Figure 46 Diagram showing the effect of the heart rate on the inequality between the refractory periods of the atrioventricular node and the anomalous pathway; see text.

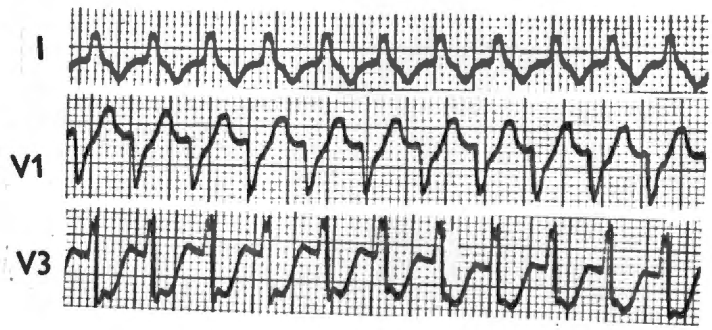


Figure 47 (Case 7) Electrocardiographic strips (leads I, V1 and V3), during paroxysmal supraventricular tachycardia. Note marked ST depression in V3.

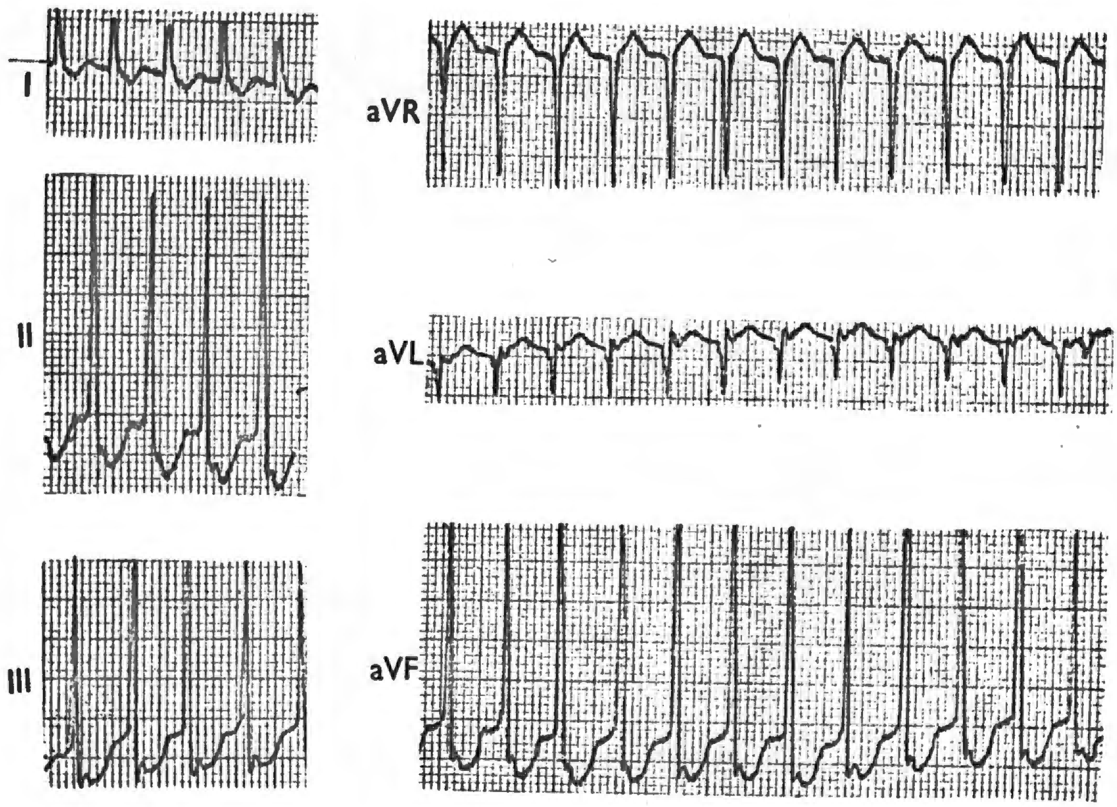


Figure 48 (Case 11) Electrocardiogram (limb leads) during paroxysmal tachycardia.

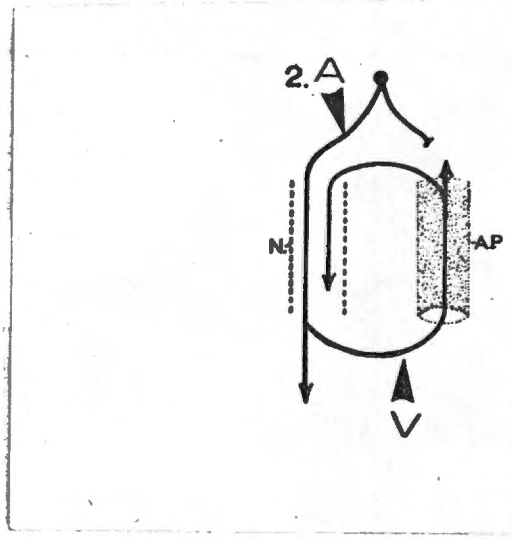


Figure 49 Diagram to show entry of extra-systoles into reciprocal pathway in Wolff-Parkinson-White syndrome.

A = supraventricular extrasystole

V = ventricular extrasystole

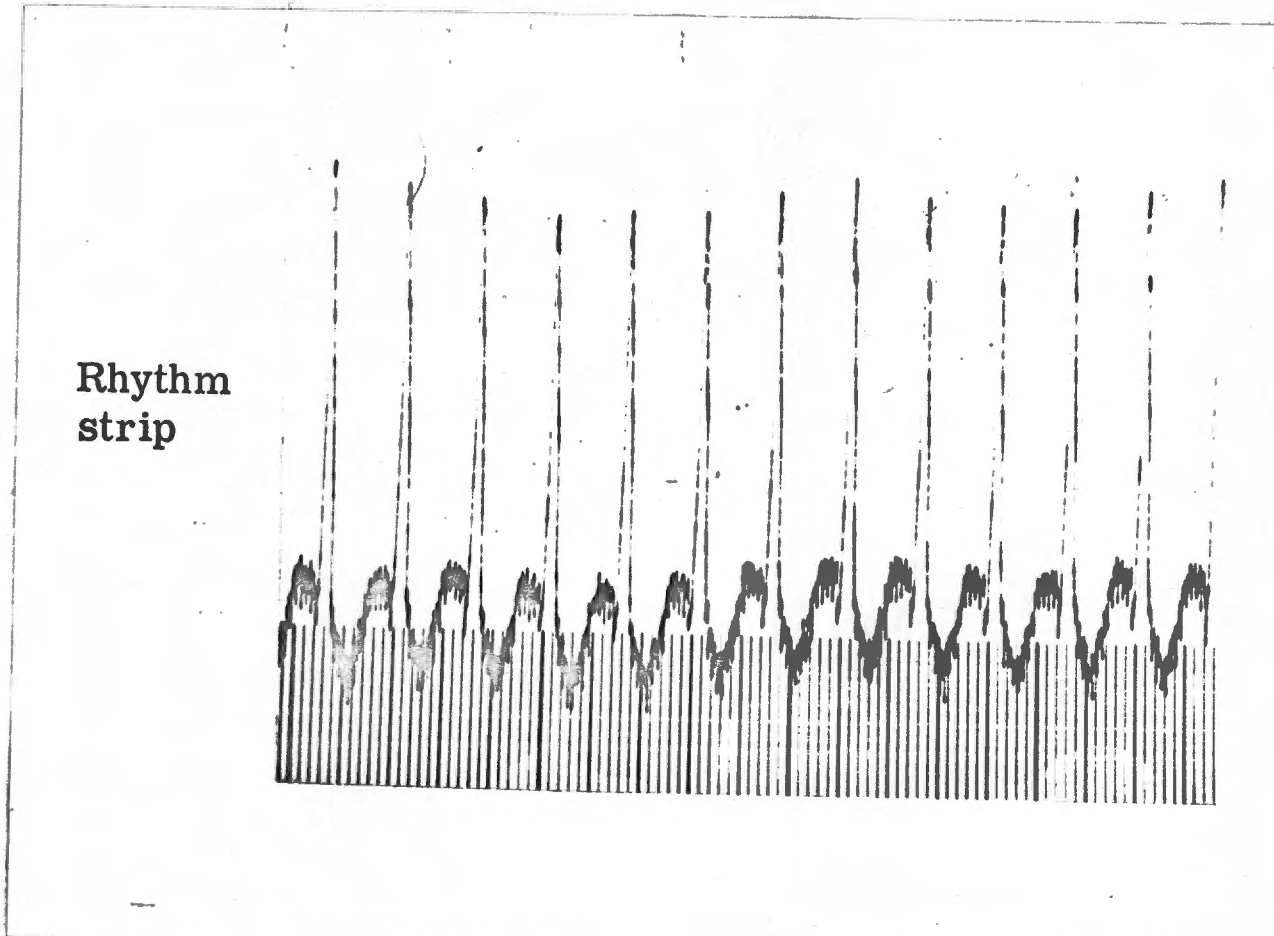


Figure 50 (Case 5) Electrocardiogram strip showing paroxysmal supraventricular tachycardia induced during His bundle electrography (200 beats a minute).

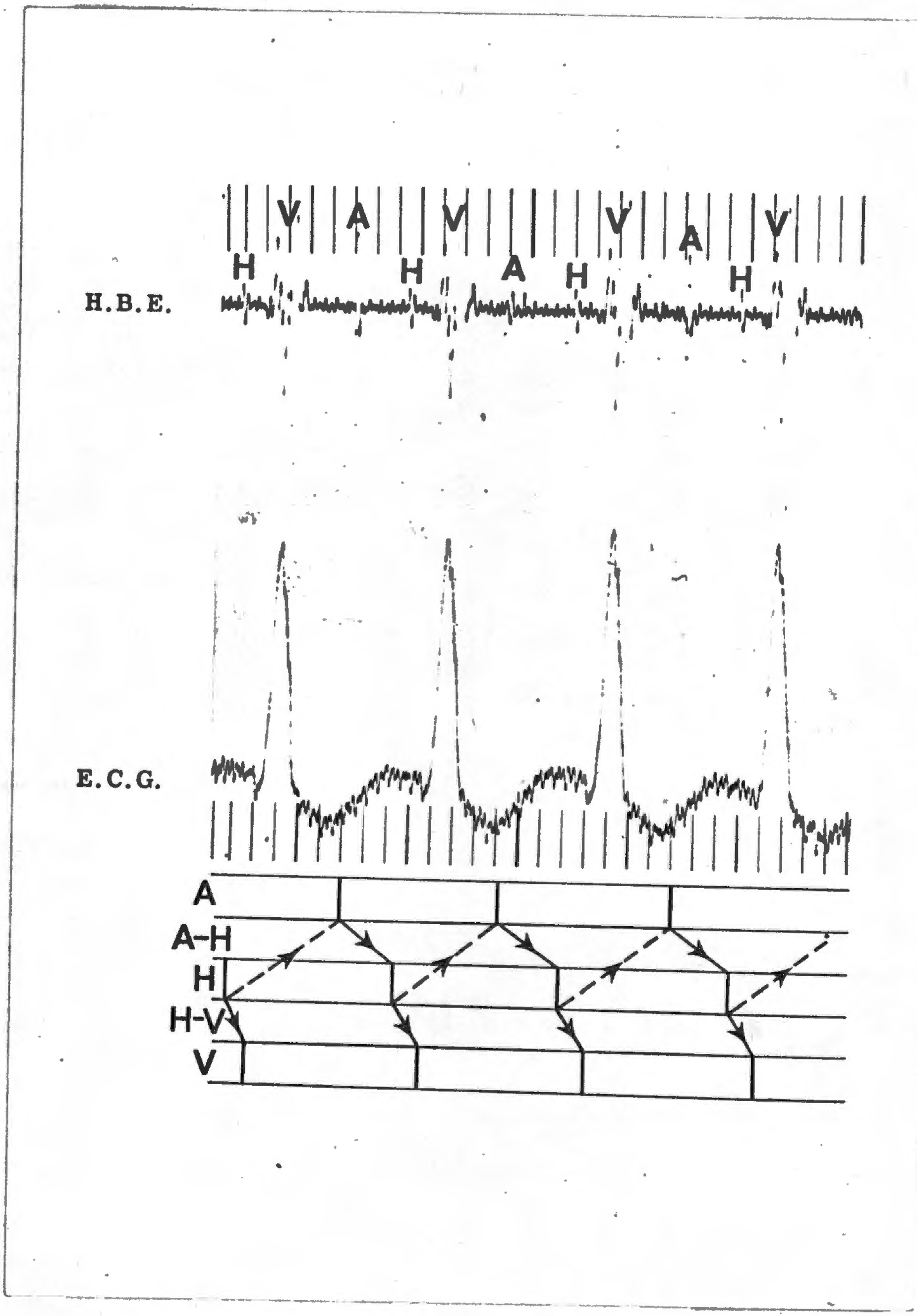


Figure 51 (Case 5) Simultaneous His bundle electrogram (upper strip), electrocardiogram (lower strip) and ladder diagram (bottom panel), during paroxysmal tachycardia.

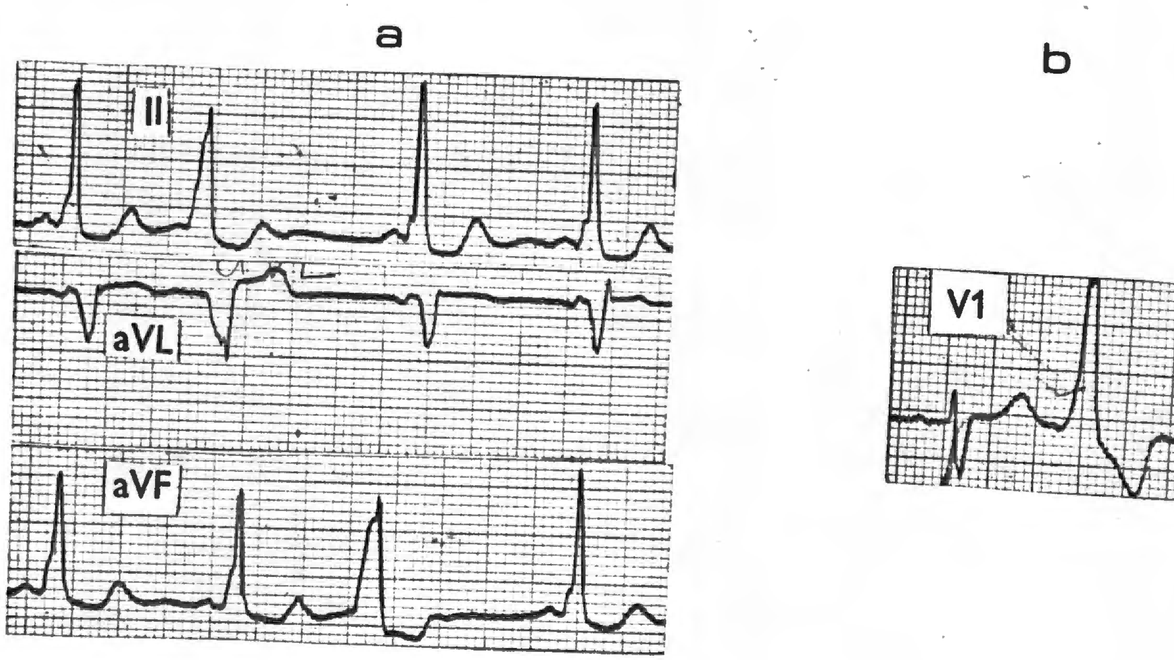


Figure 52 (Case 5) Electrocardiographic strips

(a) ventricular extrasystoles complicating pre-excitation

(b) ventricular extrasystoles during spontaneous normalization

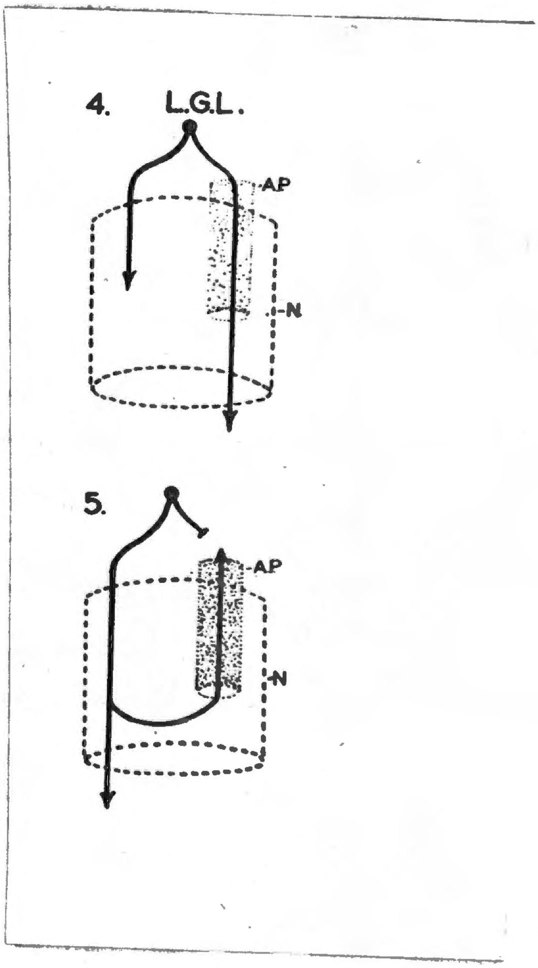


Figure 53 Diagram to show conduction pathways in Lown-Ganong-Levine syndrome during sinus rhythm (2) and during paroxysmal tachycardia (5). (Extracted from Figure 45)

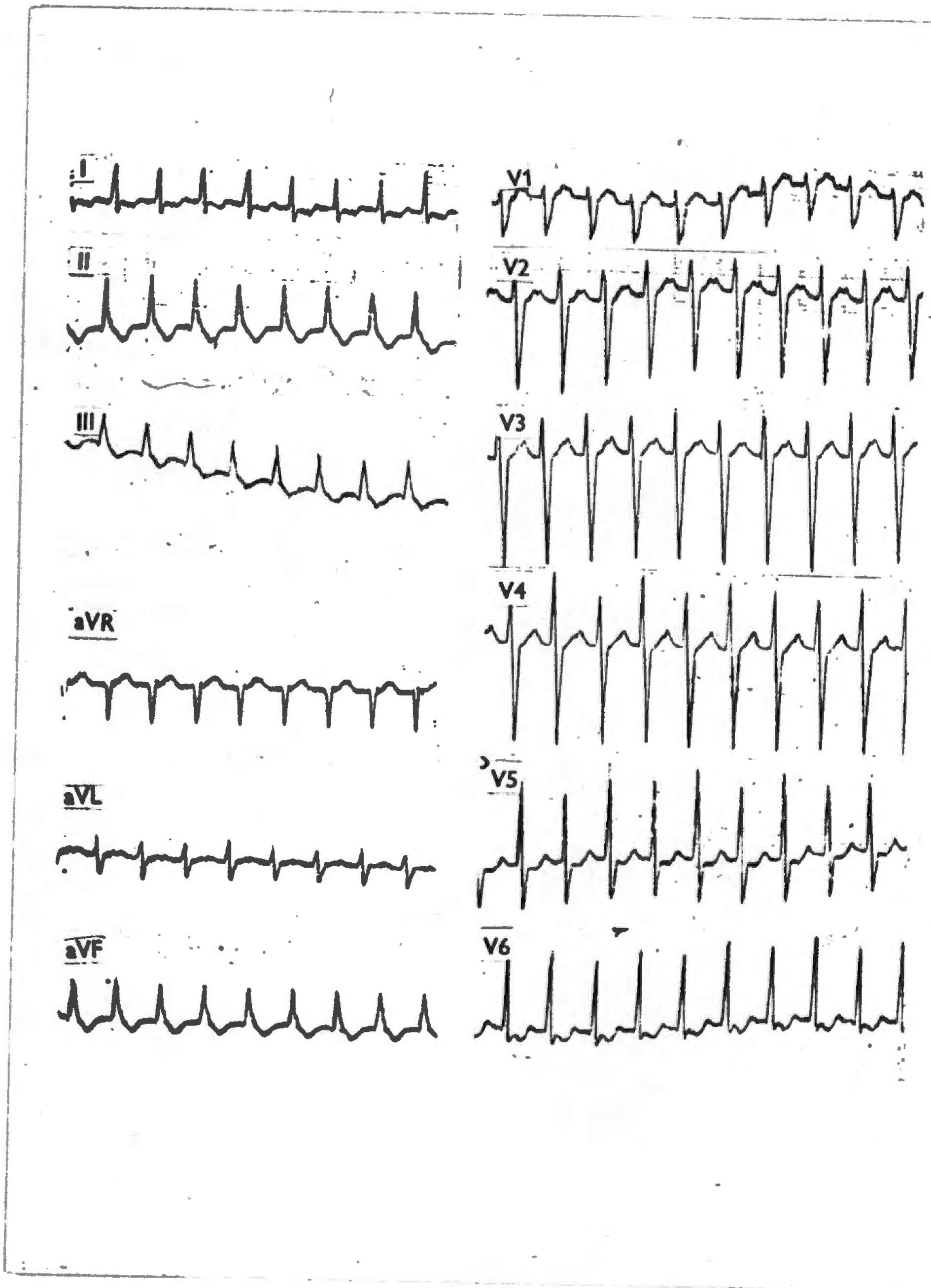


Figure 54 (Case 17) Electrocardiogram showing paroxysmal supraventricular tachycardia.

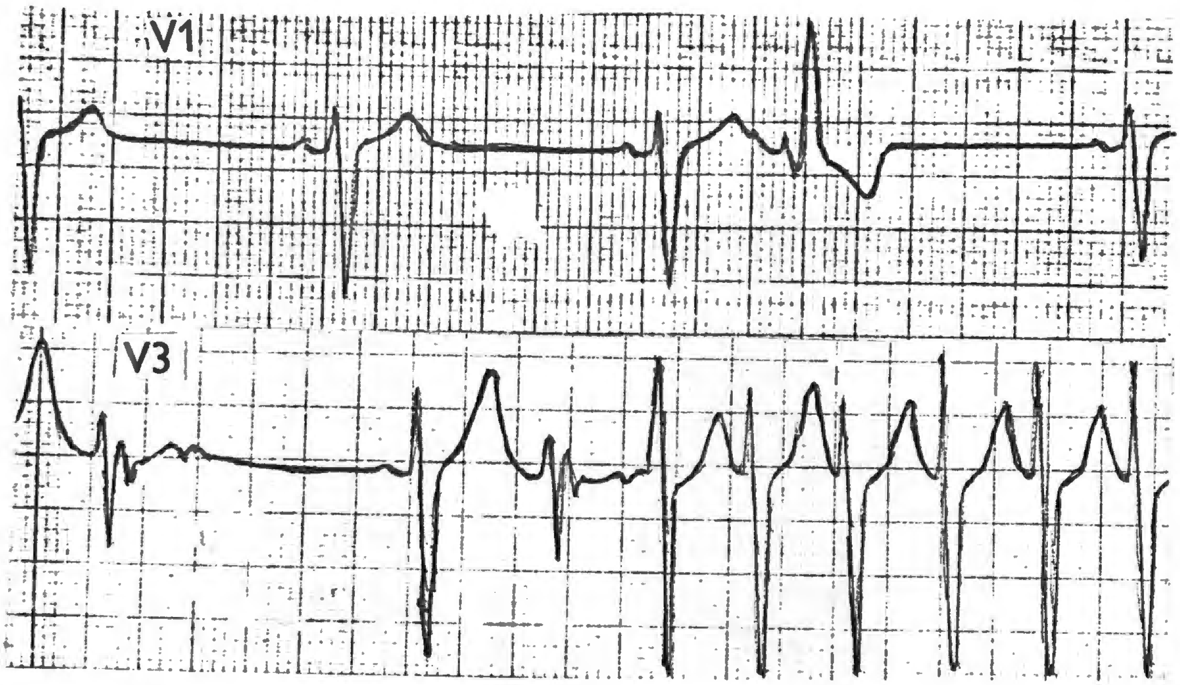


Figure 55 (Case 16) Electrocardiographic strips showing:

(a) V1, in sinus rhythm, with the third normal QRS complex followed by atrial extrasystole with aberrant conduction.

(b) V3 showing onset of paroxysmal tachycardia.

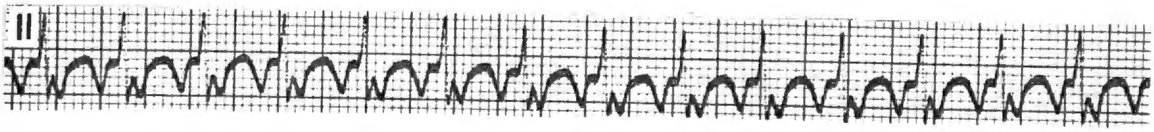


Figure 56 (Case 16) Electrocardiographic strip (lead II) showing atrial flutter.

CHAPTER 9

The Problem of Atrial Fibrillation

Atrial fibrillation may, as will be discussed, be hazardous in those with the Wolff-Parkinson-White syndrome, and frequent in the Lown-Ganong-Levine syndrome (Coumel, 1972); there may be a link between the latter and lone atrial fibrillation. Its genesis under these circumstances requires careful consideration.

The mechanism of atrial fibrillation

Electrophysiologically, both atria act as one chamber and will be referred to as the "atrial chamber". When all the fibres of the atrial chamber are in a state of complete recovery, or in a state of absolute refractoriness, they are said to be "in-phase" with each other. In myocardial fibrillation, the fibres are "out-of-phase" with each other and the chamber is fragmented electrophysiologically into numerous irregularly-shaped areas or islets in states of excitation, or partial or complete recovery. The initiation of this state is favoured by the coincidence of two basic events:

1. Uneven recovery of the chamber
2. Early impulse formation

With uneven recovery of the chamber, the fibres will be temporarily "out-of-phase" with each other during part of the cardiac cycle. If, under these circumstances, an early impulse is introduced into the chamber, it will only stimulate those fibres which have recovered, and the "out-of-phase" state is thereby accentuated. The introduction of further premature impulses into the "out-of-phase" chamber will aggravate the situation. The advancing excitation front consequently becomes very complex as it meets tissue areas in various stages of recovery, and becomes serrated with irregular digitations of excitable tissue. And as this serrated wave front meets more complex zones of uneven recovery, its digitations become longer, more bizarre and sinuous, until they ultimately fragment. The excitation and refractory zones are eventually completely fragmented into a chaotic mosaic of milling islets in various stages of recovery and excitation - the condition of established fibrillation.

Uneven recovery of the atrial chamber - the basic prerequisite to fibrillation - is favoured by four factors:

(a) longitudinal activation of the atrial chamber (in contrast to transverse activation of the ventricular chamber); (b) a large atrial mass; (c) a shortened refractory period; and (d) a prolonged conduction time. Furthermore, once established, the maintenance of fibrillation is favoured by a large atrial mass.

Early impulse formation in or to the atria - the second basic prerequisite to fibrillation - may be brought about by four mechanisms. (i) extrasystoles; (ii) tachycardia; (iii) a circus movement within the atria; and (iv) a reciprocal mechanism. In both the Wolff-Parkinson-White and Lown-Ganong-Levine syndromes, a reciprocal mechanism exists for the premature entry of a stimulus into the atrial chamber during an out-of-phase period, through the anomalous pathway. Of course, such cases are also vulnerable should atrial extrasystoles occur at the appropriate time (Bennett and Pentecost, 1970).

Figures 45, panel 3, and 57B show the situation when sinus impulses are conducted through the atrioventricular node with first-degree atrioventricular block. Any returning impulse, coming up the anomalous pathway, reaches the atria when they are completely recovered, and the atria are activated retrogradely. Further onward transmission of the impulse, down the atrioventricular node, may lead to a reciprocal tachycardia. This is not to imply that the anomalous pathway utilized under these circumstances is anatomically identical with the pathway present in the Wolff-Parkinson-White syndrome; longitudinal dissociation in the atrioventricular node may apply here (Moe and Mendez, 1966).

In the Wolff-Parkinson-White or Lown-Ganong-Levine syndromes, if the returning impulse reaches the atrial chamber during its early stage of recovery, when it is out of phase (Figure 57,B) the introduction of this early impulse into the atrial chamber may initiate atrial fibrillation. Alternatively, a very early extrasystole, occurring in the same period, may likewise initiate atrial fibrillation (Bennett and Pentecost, 1970). However, while atrial fibrillation may be reasonably well tolerated under normal circumstances, the existence of an anomalous pathway provides the mechanism for a situation of extreme hazard in cases of the Wolff-Parkinson-White syndrome. Now it is possible for the fibrillating atria to convey the impulses directly through the anomalous pathway into a localized area of ventricular myocardium.

In the Lown-Ganong-Levine syndrome, the presumed pathway through which the impulses will reach the ventricles will be either the atrioventricular node or the posterior internodal tract: in either case, unprotected ventricle will not be the recipient area.

Atrial fibrillation proved incapacitating in Case 7. In Figure 58, the rhythm is grossly irregular in the strips of V1 and lead II shown, which are representative tracings. The R-R intervals vary between 0.22 and 0.44 seconds, indicating a cardiac rate of 136-273 beats a minute. The QRS complexes are bizarre, with slurring of the upstroke of the R wave in most leads, but no P wave activity is present. In lead II the changes are exactly the same with the exception that the eighth and ninth QRS complexes reveal normalization of intraventricular conduction. These changes indicate the presence of atrial fibrillation, and the bizarre QRS complexes show that the ventricle is activated by those fibrillation impulses that are conducted through the anomalous pathway only; thus the QRS complex is made up entirely of a delta wave. They can be seen to be quite different from the contour of the QRS complexes in sinus rhythm (Figures 9 and 10) or during paroxysmal supraventricular tachycardia (Figure 47). The contrast with the latter arrhythmia is shown in Figure 59. As shown in V1 (Figure 58), the ventricular depolarization taking place exclusively by the anomalous pathway during atrial fibrillation in this case yielded a positive (delta) complex; this is in keeping with the fact that the patient suffers from the Wolff-Parkinson-White syndrome type A.

The appearances during atrial fibrillation had initially led to the diagnosis of paroxysmal ventricular tachycardia. Levine and Beeson (1941) reported three cases of Wolff-Parkinson-White syndrome who had appearances closely resembling those seen in Case 7. They considered their patients to have ventricular tachycardia, but examination of their tracings reveals them to be clearly recognizable as being due to atrial fibrillation in the Wolff-Parkinson-White syndrome. Littmann and Tarnower (1946) recognized atrial fibrillation in one of their nine cases with the Wolff-Parkinson-White syndrome, and disagreed with the previous interpretation. Since then, this has been appreciated as an important pitfall to avoid in the diagnosis of cardiac arrhythmias (Langendorf et al., 1952; Carlsten et al., 1954) though not all have taken note of this, and erroneous reports are seen from time to time (Fleishman, 1952). In an important paper that clearly analyses this problem, Yahini et al. (1964) report five patients who undoubtedly had the Wolff-Parkinson-White syndrome complicated by atrial fibrillation. As in Case 7, the complexes in general were bizarre and differed somewhat from the Wolff-Parkinson-White configuration during sinus rhythm. They too show tracings of atrial fibrillation in which occasional complexes are different from those in the remainder of the strips, as well as from tracings taken during sinus rhythm with the Wolff-Parkinson-White pattern; these indicate occasional total anterograde conduction down the normal pathway.

It has recently been suggested that Wolff-Parkinson-White syndrome is complicated by atrial fibrillation only when there is type A conduction (Chung et al., 1965).

Loew (1971) has now published a case of atrial fibrillation complicating the Wolff-Parkinson-White syndrome type B, which he believes to be the first in the literature. This statement is however incorrect, for two of the five cases of Wolff-Parkinson-White syndrome complicated by atrial fibrillation reported by Yahini et al. (1964) had type B Wolff-Parkinson-White conduction during sinus rhythm. Some doubt must therefore be cast on the basis for this claim for, as Loew (1971) points out, no reason has been advanced as to why the group B pattern should not be associated with paroxysmal atrial fibrillation. One that might bear consideration, if more series show a heavy preponderance of type A conduction in those who have atrial fibrillation, is that a left-sided bypass might, during retrograde conduction, introduce the impulse more easily at a time when the atrial chamber is out-of-phase (Figure 57, B). The "atrial chamber" usually functions as a whole (Schamroth and Krikler, 1967b), but atrial dissociation with unilateral atrial fibrillation preceding complete atrial fibrillation has been described by Chung (1971). As the sinoatrial node lies in the right atrium, it is not entirely beyond the bounds of possibility that the left atrium might be more vulnerable to fibrillation-inducing stimuli than the right.

The danger of ventricular fibrillation

When supraventricular tachycardias occur in those who do not have an anomalous pathway, the atrioventricular node is the sub-station through which all impulses that reach the ventricles have to pass. At a certain stage, the atrioventricular node ceases to respond to all impulses that reach it from the atrial chamber. In normal subjects, the P-R interval is prolonged when the heart rate is increased by atrial pacing, and this is due to progressive prolongation of the A-H time (Narula et al., 1970a), culminating in Wenckebach periods.

The application of this to the clinical study of supraventricular arrhythmias is important. In paroxysmal supraventricular tachycardia, the usual atrioventricular conduction is 1:1, provided the rate of the tachycardia is less than 200 beats a minute; with rates above this, there is usually complicating second-degree atrioventricular block (Schamroth, 1971a).

The same situation applies with atrial flutter, where the atrial rate is usually over 220 beats a minute. Here the rate is too great for the atrioventricular node to conduct each impulse, and the consequence is some degree of second-degree atrioventricular block. This is usually acompanied by a 2:1 conduction ratio, but greater degrees of block may occur. In atrial fibrillation, the usual situation is a varying second-degree atrioventricular block, due to varying degrees of penetration of the impulses conducted from the atria; this concealed conduction tends to modify the refractory period of the atrioventricular node, and this variation results in the total irregularity of ventricular response characteristic of untreated atrial fibrillation.

When we come to the Wolff-Parkinson-White and Lown-Ganong-Levine syndromes, the important feature determining the ventricular response is whether or not the impulse passes anterogradely down the normal pathways, or down the anomalous pathway. If the impulse passes down the normal pathway, it will meet the filtering mechanism of the atrioventricular node.

When the refractory period of the atrioventricular is reached by these stimuli, it will manifest a degree of block, and the ventricles will be protected from the excessively frequent impulses produced or conducted from above. In some cases of paroxysmal tachycardia, it is possible that the pathway of excitation may be in reverse of the usual; for instance, an atrial extrasystole may be blocked in or near the atrioventricular node but conducted to the ventricles through the bundle of Kent, with retrograde activation of the atrioventricular conduction system, and atrial activation, by way of the atrioventricular node (Durrer et al., 1967). Thus one can envisage the possibility of paroxysmal supraventricular tachycardia with wide QRS complexes, with rapid conduction into a localized part of a ventricle, due to the lack of interposition of the anterograde blocking mechanism of the atrioventricular node. The same consideration would apply with atrial flutter, but it is of the greatest importance in the atrial fibrillation that may complicate the Wolff-Parkinson-White syndrome. This indeed may be the explanation for sudden death in some patients who suffer from the Wolff-Parkinson-White syndrome.

In the Wolff-Parkinson-White syndrome complicated by atrial fibrillation, the varying and protective degree of atrioventricular block conferred by the atrioventricular node is lacking; as can be seen in Case 7, the vast majority of the impulses are conducted anterogradely down the anomalous pathway, producing localized depolarization of the area into which the anomalous pathway is inserted. This is manifested as the bizarre QRS complexes made up exclusively of delta waves. As can be seen in Figures 58 and 59, the appearances are different from those that occur during supraventricular tachycardia, and during sinus rhythm with anomalous conduction. The effect of this is to bombard an area of ventricular myocardium with an incessant spate of stimuli, to which it may be vulnerable, and to which haemodynamic response is poor because of the lack of efficient depolarization of the ventricles as a whole. Under these circumstances, ventricular fibrillation may occur. Seven cases of this have been documented, including one case in which the precise onset of the ventricular fibrillation was demonstrated (Dreifus et al., 1971a). Their patient had the Wolff-Parkinson-White syndrome, type A, and had previously suffered many attacks of paroxysmal supraventricular tachycardia with normal QRS complexes. She was seen on this occasion in atrial fibrillation with a ventricular rate of 190 beats a minute. These workers comment that the QRS complexes were wider and more bizarre, but that they could not see evidence of actual delta waves. Indeed, what they do publish shows that the delta waves made up the whole of the QRS complex, and the appearances were very similar to those seen in Figure 58.

They treated their patient with intravenous propanolol and digoxin; after the third dose of digoxin she lost consciousness, and the onset of ventricular fibrillation was identified. This was stopped with a direct current counter-shock, but more digoxin was given, and a second episode of ventricular fibrillation occurred. The patient was treated with more digoxin, as well as with quinidine, lignocaine, and, finally a demand pacemaker.

There can be little doubt that, in this patient, the absence of the blocking mechanism of the atrioventricular node permitted the development of ventricular fibrillation when the ventricles were bombarded by impulses from the fibrillating atria, down the anomalous pathway. This is obviously of greater danger to patients with the Wolff-Parkinson-White syndrome; the greatest risk in the development of an arrhythmia is that it will enter the ventricles through the anomalous pathway and that it may then precipitate ventricular fibrillation. The fact that ventricular fibrillation did not recur, even though digoxin was continued, may well have been due to the concomitant administration of other anti-arrhythmic agents, including propanolol, quinidine and procainamide. It is important to stress that digoxin should be avoided in cases of atrial fibrillation when the Wolff-Parkinson-White syndrome is suspected. The finding of bizarre QRS complexes like those seen in Figure 58; an unduly rapid ventricular rate (implying the lack of the protective mechanism of the atrioventricular node); and the availability of previous electrocardiograms showing the Wolff-Parkinson-White syndrome: these observations should lead to extreme caution in the use of what would otherwise be an entirely acceptable form of therapy in atrial fibrillation.

However, even without the administration of digitalis, atrial fibrillation may lead to ventricular fibrillation, at least as judged by experiences with a dog who suffered from the Wolff-Parkinson-White syndrome (Boineau and Moore, 1970) (see Chapter 4). This case, albeit in an animal, illustrates the vulnerability of the ventricle to rapid stimuli transmitted down an anomalous pathway, when not filtered and partially blocked by the intervention of the atrioventricular node.

The reasons for the effect of digitalis under these circumstances have been considered by Wallace et al. (1971). Digitalis, as mentioned previously, has for long been known to prolong the effective refractory period of the atrioventricular node. It also is known to shorten the refractory period of atrial muscle. An anomalous pathway taking the form of the bundle of Kent is made up of muscle fibres.

If these have electrophysiological characteristics similar to those of atrial muscle, and if they are supplied by the vagus nerves, it is plausible that digitalis will actually shorten the refractory period of this anomalous pathway. Under circumstances of atrial fibrillation, the effect would be an increase in the maximal ventricular rate. We would then not merely be dealing with diversion of atrial impulses because of the physiological block of the atrioventricular node induced by the atrial fibrillation, or because the initial impulse that established the atrial fibrillation may have entered the atrial chamber retrogradely near the atrioventricular node, in the process rendering it refractory; there may well thus be an active mechanism whereby digitalis promotes conduction down the anomalous pathway. The delta waves seen in atrial fibrillation complicating the Wolff-Parkinson-White syndrome do in any case represent localized preexcitation; under these circumstances there is usually little, or more usually none, of the contribution to ventricular depolarization from stimuli passing down the bundle of His; and with digitalis the rate as well as the quantity of the impulse passing down the anomalous pathway would be increased. Under these circumstances, the risks of ventricular fibrillation may be increased. The consistent precipitation of ventricular fibrillation following the induction of atrial fibrillation in a dog with the Wolff-Parkinson-White syndrome reported by Boineau and Moore (1967) is instructive and will be further discussed in Chapter 11.

One can speculate that this could be a cause of sudden unexpected death; at autopsy no cause will be found unless there was reason to suspect the Wolff-Parkinson-White syndrome and detailed studies undertaken (Davies, 1971). In Chapter 11, this will be further discussed with reference to the absence of the signs of pre-excitation during sinus rhythm.

In the Lown-Ganong-Levine syndrome, impulses will travel into the ventricles in a more normal fashion than in the Wolff-Parkinson-White syndrome, down the bundle of His and the bundle branches. It is thus not to be expected that such cases will be at risk of ventricular fibrillation, as in the case of the Wolff-Parkinson-White syndrome.

Lone atrial fibrillation

Atrial fibrillation may occur in the absence of organic heart disease (Mohler and Lintgen, 1931; Phillips and Levine, 1949) and has been termed "lone auricular fibrillation" (Evans and Swann, 1954). About 5-6% of all cases of atrial fibrillation fall into this category (Friedlander and Levine, 1934; Orgain et al., 1956). While Bellet (1971) considers coronary artery disease to be the cause, this has not been substantiated and there is much evidence to the contrary. Thus, lone atrial fibrillation usually occurs in young individuals who have no evidence of coronary artery disease, as exemplified by the 44-year follow-up of a case in whom subsequent autopsy showed normal coronary arteries (Levine, 1963). There have also been several reports of a familial incidence (Levy, 1942; Wolff, 1943). Gould (1957) found 22 cases in a family of 113 members during a period of observation of 36 years; Friedberg (1966) encountered the arrhythmia in a man, his brother and his son; it has also been seen in an uncle and his nephew (Schamroth and Krikler, 1967b).

Evans and Swann (1954) exclude cases of paroxysmal atrial fibrillation "in the belief (emphasis added) that it is a separate entity". The distinction is, however, artificial, for there is no evidence whatsoever to support this supposition. This was recognized by Wood (1956) who states quite clearly that "lone auricular fibrillation" may be paroxysmal or permanent. The term "lone atrial fibrillation" can thus refer to any form of atrial fibrillation - paroxysmal or established - in which there is no evidence of associated organic heart disease.

It has already been indicated that, in both the Wolff-Parkinson-White and Lown-Ganong-Levine syndromes, the rapidly-returning retrograde impulse may reach the atrial chamber when it is out-of-phase, and that the P-R interval is not consistently short in all cases of the Lown-Ganong-Levine syndrome at all times. It is thus a reasonable hypothesis that in at least some cases "lone atrial fibrillation" is due to retrograde conduction through an anomalous pathway analogous to the Lown-Ganong-Levine syndrome.

Might some cases of lone atrial fibrillation be due to an "occult" or "concealed" Wolff-Parkinson-White syndrome, to be discussed in Chapter 11, rather than the variation of the Lown-Ganong-Levine syndrome, as here postulated? The answer must be no, for the reason that, in lone atrial fibrillation, the QRS complexes are normal. Therefore, anterograde conduction must occur through a pathway entering the bundle of His, and thus leading to narrow, normal-looking, QRS complexes. Were "occult Wolff-Parkinson-White syndrome" the explanation, one would see bizarre irregular delta waves, as in case 6 of Yahini et al. (1964).

There was no evidence of organic heart disease to cause the paroxysmal atrial fibrillation in Case 18. An electrocardiogram (Figure 60) (taken while on digoxin) shows sinus rhythm at the rate of 54 beats a minute. Sagging ST segments are present in leads I, II, aVF, V5 and V6. There are small Q waves, within the limits of normal, in leads I, II, aVF, V5 and V6. The P-R interval was 0.14 seconds, and the QRS interval, 0.08 seconds. The P waves are peaked in some leads e.g. I, II, aVF and aVR (albeit inverted in the latter), biphasic in V1, and bifid in V3, V4 and V5. There are no QRS changes indicative of cardiac ischaemia. The abnormalities in the P wave suggest the possibility of intra-atrial conduction disturbance. The sagging ST segments are explicable on the basis of digitalis effect.

Figure 61 shows tracings in the same patient (a) during sinus rhythm, with atrial extrasystoles following the first and last sinus beats; (b) atrial fibrillation; and (c) atrial fibrillation, with the ventricular response slowed after intravenous verapamil (see Chapter 10).

Atrial fibrillation is thus a disorder of varied manifestation in the pre-excitation syndromes: potentially a great hazard when it complicates the Wolff-Parkinson-White syndrome; troublesome, but theoretically at least less dangerous in the Lown-Ganong-Levine syndrome; and very likely arising on the basis of a similar mechanism to the Lown-Ganong-Levine syndrome, in at least some cases of lone atrial fibrillation.

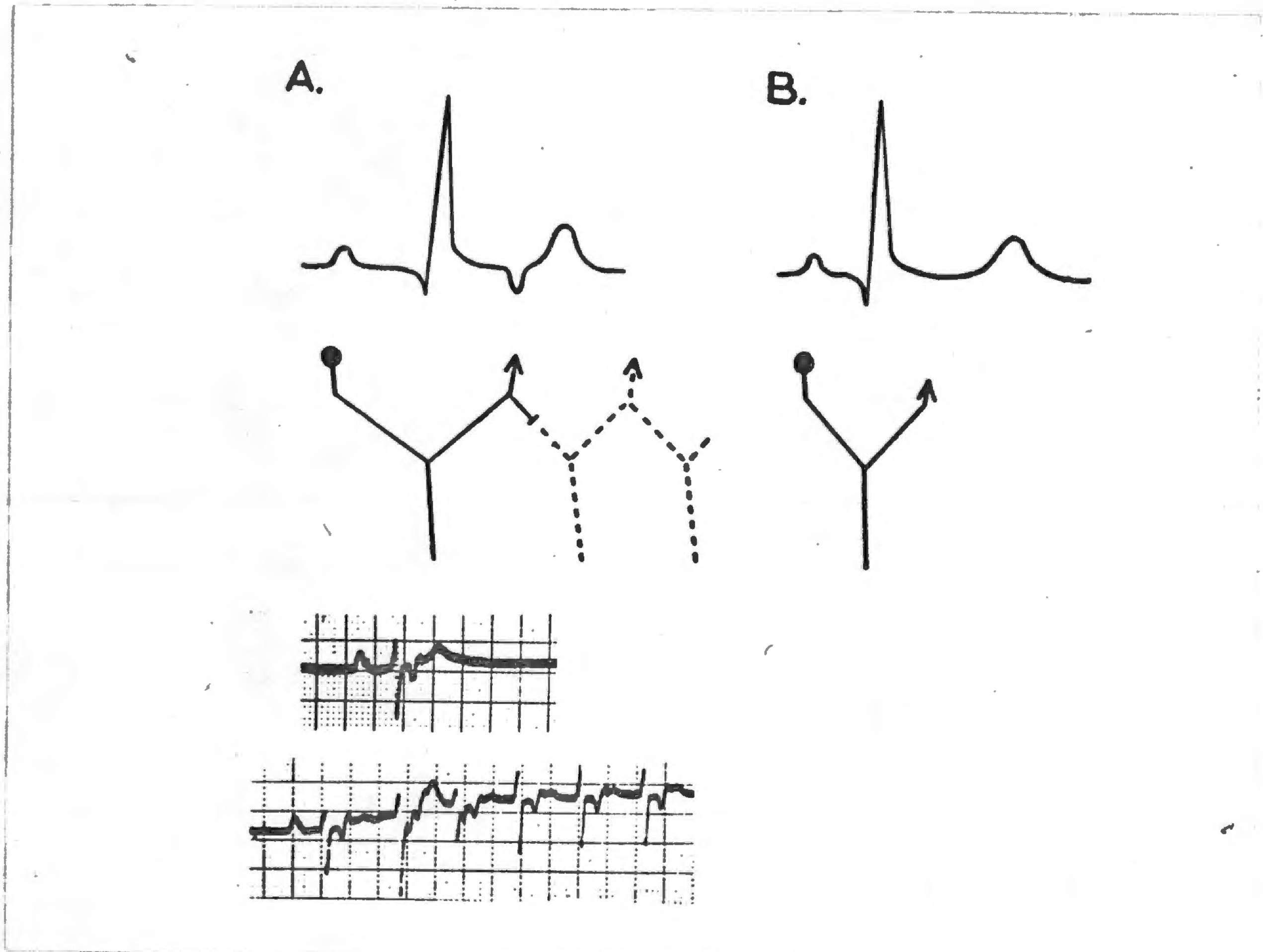


Figure 57 Diagram showing the effect of the reciprocal return to the atria of a sinus impulse, (A) when a reciprocal arrhythmia is induced; (B) when the return impulse reaches the atrial chamber during the early stage of recovery.

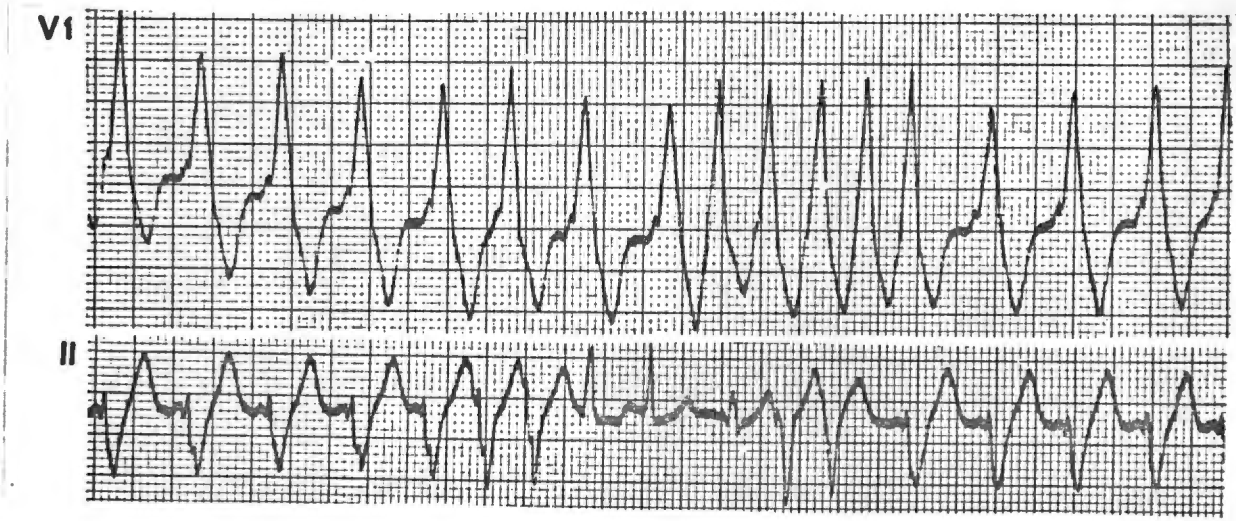


Figure 58 (Case 7) Electrocardiographic strips (V1 and II) showing atrial fibrillation.

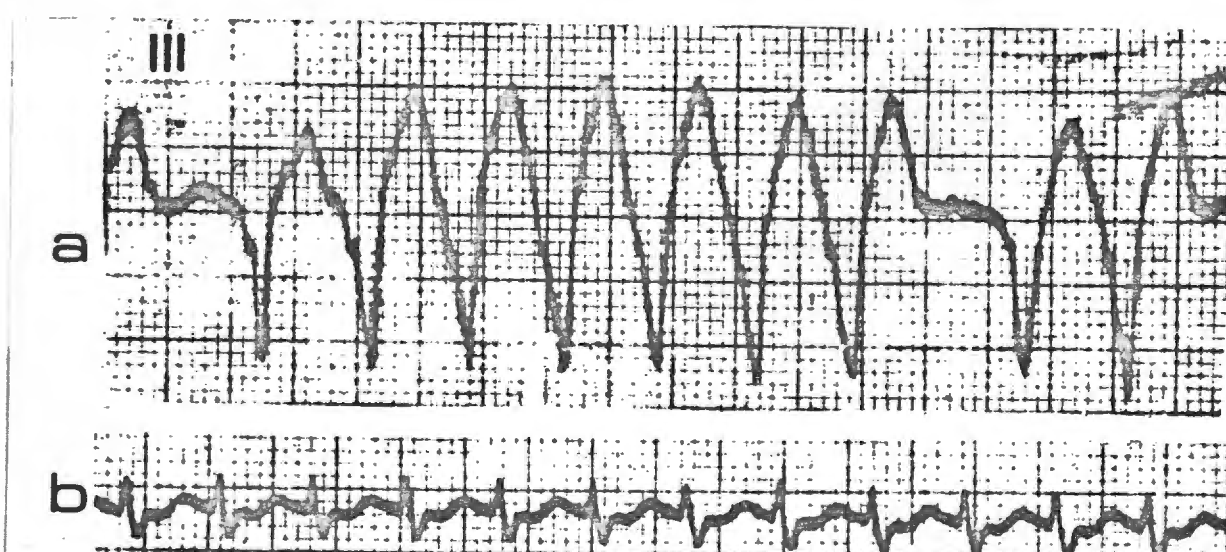


Figure 59 (Case 7). Electrocardiographic strips (leads III) showing (a) atrial fibrillation (b) paroxysmal supraventricular tachycardia.

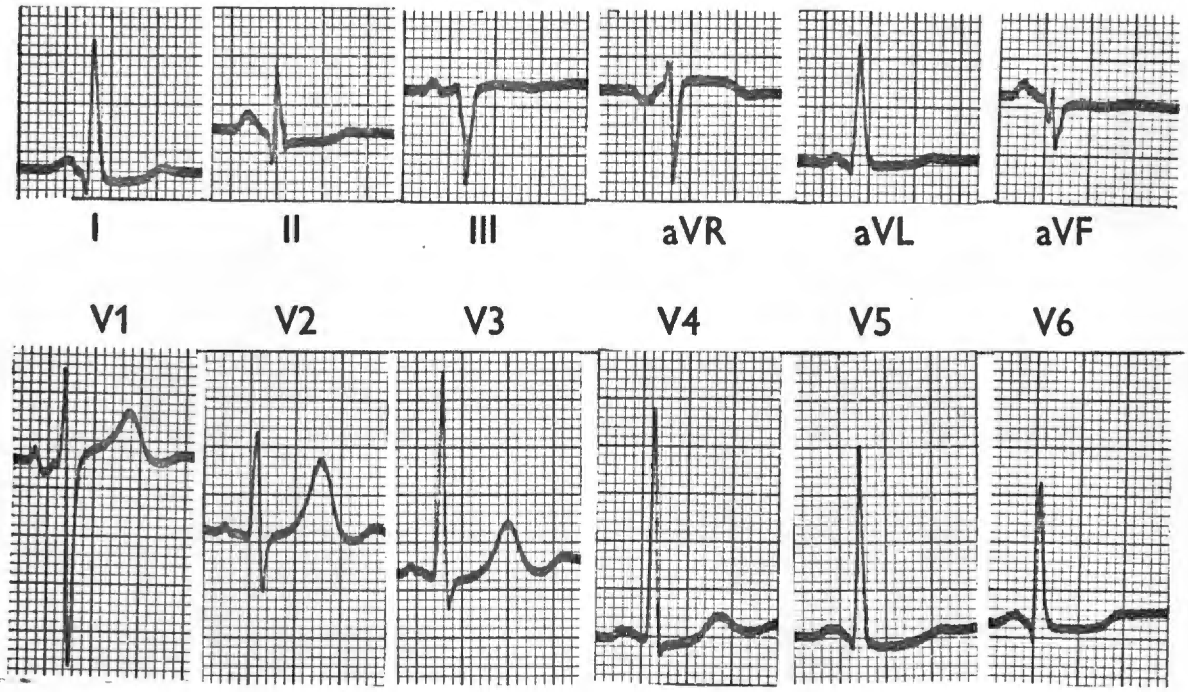


Figure 60 (Case 18) Electrocardiogram, showing sinus rhythm.

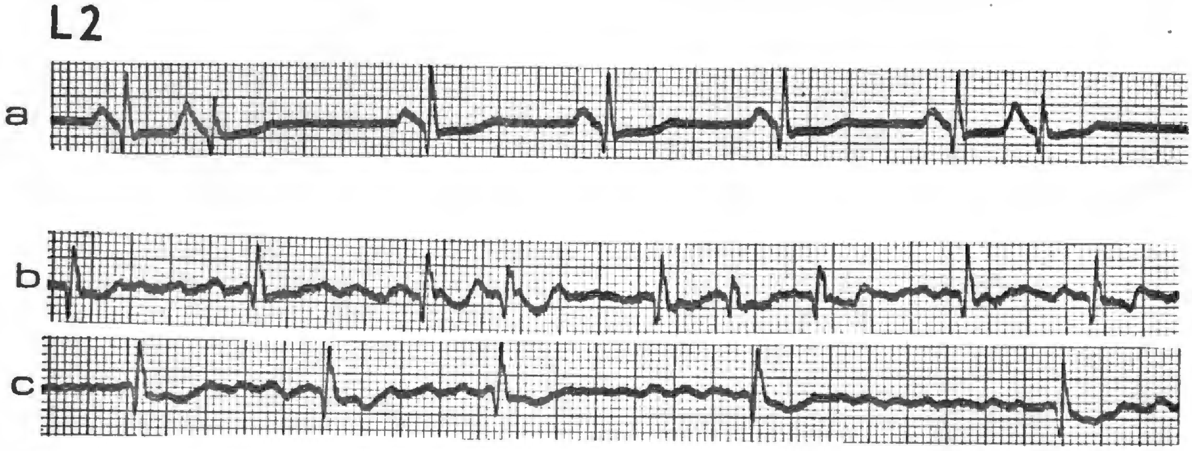


Figure 61 (Case 18) Electrocardiographic strips showing

(a) sinus rhythm, with atrial extrasystoles
(b) atrial fibrillation
(c) atrial fibrillation, after verapamil.

CHAPTER 10

Aspects of the Treatment of Arrhythmias Complicating Pre-excitation

It is not proposed to analyse in detail the management of arrhythmias related to pre-excitation, but rather to touch on the main points before considering certain specific developments. The principles are important: obviously, attacks must be controlled, but also steps may need to be taken to prevent their recurrence.

For the treatment of paroxysmal tachycardia complicating pre-excitation syndromes, digitalis or quinidine may be used (Bellet, 1971), and beta-blocking agents e.g. propranolol, are often effective (Gettes and Surawicz, 1967); but vagotonic procedures like carotid sinus pressure often work well. Measures that proved useful in individual patients are mentioned in Section C. In addition, the role of verapamil will be discussed below.

The treatment of atrial fibrillation in the Wolff-Parkinson-White syndrome is a very vexed question. Some use digitalis, but others believe that this is hazardous. As one can see from the fact that the complexes during atrial fibrillation largely if not exclusively consist of delta waves, one would not wish to increase conduction down the anomalous pathway and blocking the normal pathways. As Wolff and White (1948) have pointed out, digitalis is capable of prolonging or completely blocking conduction at the atrioventricular node, while it apparently favours anomalous atrioventricular conduction without changing the transmission interval. Yahini et al. (1964) believe that it is rational therapy to try quinidine or procainamide first because paroxysmal ventricular tachycardia cannot always be excluded with absolute certainty; and this may well be reasonable advice to those who are uncertain, perhaps modified in that lignocaine might be more acceptable to-day. One may seriously question the wisdom of giving digitalis in the case reported by Dreifus et al. (1971a): it seems likely that this, by enhancing anomalous conduction into an area of ventricle "unfiltered" by the atrioventricular node, may have initiated the ventricular fibrillation. Digitalis therapy may be an added risk in atrial fibrillation complicating the Wolff-Parkinson-White syndrome even though Yahini et al. (1964) gave it with satisfactory results in converting the arrhythmia to sinus rhythm in two of their six cases. On this basis they aver that, if quinidine or procainamide fail, "digitalis may be added without concern". This appears to be unwise, for reasons stated in Chapter 9. Whether or not verapamil will be subject to the same hazards as digitalis remains to be tested; it may well be unsafe (see below). If a patient is distressed, direct-current defibrillation would seem to be the rational form of therapy to try. Indeed, for intractable tachycardia not responding to drugs, direct-current cardioversion has been successful (Knoebel et al., 1963; Cufforth and Newman, 1965; Hayton and Lopez, 1968) and was employed to terminate one episode of atrial fibrillation in Case 7. Stimulated intracardiac (direct atrial or ventricular) depolarization may interrupt the reciprocating pathway and has been used in order thereby to stop a paroxysm of tachycardia (Durrer et al., 1967; Durrer, 1968; Massumi et al., 1970). This has been extended by the use of a permanent demand pacemaker in order to achieve the same purpose - in an adult (Ryan et al., 1968) and in an infant (Dreifus et al., 1971b). It has been shown that a sharp thump on the chest may revert ventricular tachycardia, probably by inducing the right amount of current (Pennington et al., 1970). No documented case of this procedure in reciprocal tachycardia with Wolff-Parkinson-White syndrome has been encountered, but it is plausible that an appropriately-timed blow could, in the same way, interrupt the reciprocal cycle. This is strongly albeit indirectly supported by the fact that Case 2 has, since childhood, stopped his own paroxysms of tachycardia in this way.

When all else fails, and the arrhythmia is life-threatening, there are now certain circumstances in which surgical treatment can be considered. This derives from the direct confirmation by Durrer and Roos (1967) that the earliest activation of the ventricles in a patient with the Wolff-Parkinson-White syndrome type B was in the right lateral portion of the atrioventricular sulcus. This they showed by epicardial mapping in a patient who was undergoing closure of an atrial septal defect. The next step was when Burchell et al. (1967) undertook epicardial mapping on a man with the Wolff-Parkinson-White syndrome type B and disabling paroxysmal tachycardia. When the atrioventricular sulcus was compressed at the point of earliest activation; the tachycardia stopped, doubtless because retrograde conduction was interrupted. The delta wave was abolished by the injection of procaine into this area; this indicates that localized pre-excitation was suppressed. However, local incision into the area of the presumed anomalous pathway was unsuccessful, and the Wolff-Parkinson-White pattern returned on post-operative electrocardiograms.

The first report in which the anomalous pathway was successfully cut was that by Cobb et al. (1968); this stopped the tachycardia (and also abolished the delta waves) in a man with the Wolff-Parkinson-White syndrome type B who had developed cardiac failure because of his frequent uncontrollable attacks. He has remained free of tachycardia and without electrocardiographic evidence of the Wolff-Parkinson-White syndrome for at least 2½ years (Wallace et al., 1971). Two further successes have been reported, also in patients with type B conduction, by these same workers, with no relapse after one year and nine months respectively; in the latter case the indication for operation was syncope due to ventricular fibrillation.

However, the story is not one of unqualified success. Firstly, the procedure is more easily applicable to cases with right-sided bypasses, i.e. type B, for the left side of the heart is technically difficult to explore, whether by epicardial mapping or by surgery. With intermittent pre-excitation, precise localization of the bypass may prove impossible, and surgical treatment may fail, as instanced by Lindsay et al. (1971). Finally, despite careful mapping, Cole et al. (1970) found that resection of the apparently appropriate area failed to normalize the electrocardiogram in both their patients. To explain these failures, Lindsay et al. (1971) postulate that the pre-excitation pathway may be more diffuse than thought, that the depth of the incision may be inadequate, and that lack of pre-excitation at the time of surgery may hamper localization. To this must be added the possibility of another pathway, not identified by epicardial mapping, and yet capable of function; as discussed in Chapter 2, more than one anomalous tract may be present. This has recently been demonstrated electrocardiographically by Ramachandran (1972); though His bundle electrograms were lacking, the conclusions cannot be doubted. During paroxysmal tachycardia the QRS complexes consisted of delta waves, of type A morphology, and closely resembled Figure 58, except for the regularity of the rhythm, i.e. anterograde anomalous conduction. In this case, during sinus rhythm, type A or type B conduction was seen. It is impossible, of course, on the electrocardiogram alone to diagnose reciprocating tachycardia or atrial flutter in this case.

Because of the technical difficulty of mapping and then cutting the anomalous pathway in type A conduction (though this has been done successfully on two occasions according to a personal communication from H.J.J. Wellens), an alternative operation is the production of complete heart block by ligation of the area of the atrioventricular node and bundle of His; permanent pacemaker therapy was then instituted. Three successful case reports using this technique are those of Dreifus et al. (1968), Edmonds et al. (1969) and Dunaway et al. (1972).

<u>Verapamil</u>

During the course of an investigation into the immediate effects of intravenous verapamil in a variety of cardiac arrhythmias (Schamroth et al., 1972), its effect was assessed in patients whose arrhythmias were associated with pre-excitation syndromes. Verapamil (Cordilox, Isoptin, iproveratril) is α- isopropyl - α(N-methyl-N-homoveratryl) -γ-aminopropyl- 3,4, -dimethoxyphenylacetonitrile. The technique was as reported: prior to the injection, each patient rested in bed for twenty minutes, the blood pressure was measured, and a 90 second control electrocardiogram tracing was recorded. Verapamil was then injected intravenously in a dose of 10 mg., over a period of 15-30 seconds. Continuous tracings were recorded until a change in rhythm occurred.

In Case 7, with paroxysmal supraventricular tachycardia, conversion to sinus rhythm occurred 80 seconds after the completion of the injection of verapamil (Figure 62). The blood pressure was 90/70 mm.Hg prior to the injection, was unchanged immediately thereafter, and rose to 130/70 mm.Hg within 20 minutes.

The patient, who had complained of retrosternal discomfort and dyspnoea during the attack, lost these symptoms within a matter of minutes.

Case 11, with supraventricular tachycardia, was given lignocaine and practolol, but supraventricular tachycardia persisted until he was given verapamil 10 mg. intravenously, which was followed 30 seconds later by conversion to sinus rhythm (Figure 63). At the point of conversion, a ventricular extrasystole follows the tachycardia and itself is followed by a ventricular escape beat, before sinus rhythm is restored, showing QRS complexes identical with those subsequently seen during sinus rhythm. These continuous tracings are interrupted, after the fifth sinus beat, by an extrasystole and a probable reciprocal beat before sinus rhythm is finally restored. His blood pressure had been 120/80 mm.Hg before the conversion and was unchanged after it.

Case 16, who had atrial flutter with 2:1 AV block, showed conversion to sinus rhythm 136 seconds after the injection of verapamil was completed (Figure 64). There is an increase in the degree of atrioventricular block (fourth and fifth strips); transient atrial fibrillation (sixth strip); and conversion to normal sinus rhythm (bottom strip). Note short P-R interval (Lown-Ganong-Levine syndrome). His condition had been satisfactory prior to the conversion (except that his blood pressure was 90/70 mm.Hg and had on a previous occasion fallen even lower in the erect position); after conversion the blood pressure was 110/70 mm.Hg.

Case 17, also with the Lown-Ganong-Levine syndrome, responded rapidly after administration of verapamil (Reckless and Gilchrist, 1971), and showed no change in blood pressure; the level was 120/80 mm.Hg both before and after conversion.

One other patient with paroxysmal tachycardia associated with the Wolff-Parkinson-White syndrome has been reported as having responded to verapamil (Oram et al., 1971). This was a woman of 45 who had a severe paroxysm of tachycardia three years previously, that was said to have culminated in myocardial infarction. Subsequent paroxysms failed to respond to a number of agents, including digoxin, quinidine, procainamide, propranolol, practolol and sodium hydantoinate. A severe paroxysm failed to respond to direct current electroconversion, but after verapamil 5 mg. intravenously "she immediately reverted to sinus rhythm." When she relapsed five days later she responded immediately when given verapamil again. The brisk conversion to normal rhythm on two occasions, where so many other agents or measures have failed, is a further example of its usefulness under these conditions.

The results with verapamil in other arrhythmias provide indications of its action in patients with arrhythmias associated with pre-excitation syndromes. This substance was originally introduced for the treatment of myocardial ischaemia (Hoffmann, 1964; Sandler et al., 1968; Sowton, 1969). In the course of experimental work it was found to have anti-arrhythmic properties (Melville et al., 1964; Bender et al., 1966; Rodrigues -Pereira and Viana, 1968). In man, when given for cardiac ischaemia, the Wenckebach phenomenon was noted and considered to be a sign of overdosage (Bender and Zimmerhof, 1967). Its action in atrial fibrillation was investigated by Schamroth (1971b), who found it to reduce the ventricular rate and also to regularize the ventricular response.

Verapamil acts promptly by intravenous injection in many cardiac arrhythmias. Maximum blood levels are reached 3-12 minutes after injection, the concentration then falling rapidly to zero within 20-30 minutes (Melville et al., 1969). Its anti-arrhythmic action during general anaesthesia lasts about 30 minutes (Brichard and Zimmerman, 1970). Such single doses appear safe; none of the cases reported by Schamroth et al. (1972) suffered any ill-effects. Rydén and Saetre (1971) observed no significant haemodynamic effects following continuous intravenous infusion of verapamil in 10 patients in sinus rhythm. However, in two digitalized patients with atrial fibrillation there was a fall in the ventricular rate, blood pressure and cardiac output, though the stroke volume increased; verapamil has been shown not to block the effects of isoprenaline on ventricular stroke volume (Ross and Jorgensen, 1967).

The fact that Bender and Zimmerhof (1967) originally noticed the Wenckebach phenomenon when administering verapamil for cardiac ischaemia may give an important clue to its antiarrhythmic action. Others have found that it may produce varying degrees of atrioventricular block (Brichard and Zimmerman, 1970; Rydén and Saetre, 1971). Goldreyer and Bigger (1971) have shown on the basis of His bundle recordings made during paroxysmal supraventricular tachycardia, that the site of re-entry responsible for the arrhythmia was in the atrioventricular node. Their His bundle electrograms (figures 8 and 9 in that paper) show two different ways of stopping paroxysmal supraventricular tachycardia. In figure 8 they show termination of the episode of supraventricular tachycardia when a stimulated atrial depolarization was introduced at such a time as to cause marked prolongation of the A-H interval of this atrial premature depolarization. Thus by slowing conduction within the atrioventricular node beyond the critical period essential for the maintenance of re-entry, it was possible to stop the attack. In their figure 9 they show termination of sustained supraventricular tachycardia by carotid sinus massage. At first there was gradual prolongation of the conduction time across the atrioventricular node as shown by prolongation of the A-H interval. Such slight lengthening had no influence on the arrhythmia, but when the A-H interval was almost doubled, retrograde conduction failed, and sinus rhythm was resumed. It therefore seems reasonable to postulate that a possible mechanism of the action of verapamil in stopping paroxysmal supraventricular tachycardia is the prolongation of intranodal conduction to such a length as to render re-entry impossible. This would be of particularly great importance in such paroxysmal tachycardias where re-entry can clearly be associated with the occurrence of the tachycardia. The Wolff-Parkinson-White and Lown-Ganong-Levine syndromes are clearly cases in point.

In two patients in whom it was possible to convert paroxysmal supraventricular tachycardia to sinus rhythm, transient atrioventricular delays were produced prior to the conversion. Neither had evidence of underlying pre-excitation; conversion to sinus rhythm showed features that appear relevant to this subject.

The response in Case 19 is shown in Figure 65. In the control tracing, marked O, the cardiac rate is 160 beats a minute, and the R-R interval is 380 milliseconds. These values are quite constant throughout the spell of paroxysmal tachycardia observed. A clear P wave cannot be defined discreetly from the T wave.

The second strip starts 24 seconds after the completion of the injection of verapamil. The R-R interval between the first two complexes is the first one that is wider than 380 milliseconds, and is 430 milliseconds. At this stage the cardiac rate is 155 beats a minute, only a small drop from the rate of 160 during the established paroxysmal tachycardia. The third QRS complex is followed by a rather more peaked T wave which appears to contain a P wave, with a P-R interval of 340 milliseconds. The P wave can more clearly be seen to deform the T wave that follows the fourth QRS complex, and the P-R interval remains at 340 milliseconds during the succeeding five beats, then gradually lengthening. At the end of this strip, the R-R interval has increased to 520 milliseconds and the heart rate is now 115 beats a minute.

The third strip commences 48 seconds after the completion of the injection of verapamil. The first R-R interval is 640 milliseconds, the heart rate being 94 beats a minute. At the end of this strip the R-R interval has increased to 680 milliseconds and the heart rate has dropped slightly to 88 beats a minute. The P-R interval has now lengthened further, from approximately 400 milliseconds at the commencement of the strip (definition of the onset of the P wave is difficult at this stage) to 440 milliseconds at the end of the strip.

In the lowermost strip, which started 60 seconds after the completion of the injection, there was a sudden change. The heart rate is now constant throughout the strip at 78 beats a minute with an R-R interval of 760 milliseconds, the P-R interval is consistently 150 milliseconds, and the P wave has a normal appearance.

The above changes demonstrate two features. On the one hand, there is slight progressive lengthening of the R-R intervals in the second and third strips, and the P-P intervals correspond closely with the associated R-R intervals. This indicates slowing of an ectopic atrial pacemaker, or of reciprocal atrial depolarization. As these changes occur, the P-R interval also lengthens progressively, but the arrhythmia persists, albeit partially suppressed, until quite sharply there is a change to a somewhat slower atrial and ventricular rate, with a constant P-P and R-R interval, and a normal P-R interval, when the sinoatrial node regains control of the heart and once again becomes the primary pacemaker. The subsidiary pacemaker has been effectively suppressed, and atrioventricular conduction, which was progressively lengthened during the influence of the verapamil, has suddenly returned to normal once the normal pacemaker has re-established its function.

A further illustration of this phenomenon is provided by the response in Case 20. Figure 66a shows the appearances during paroxysmal supraventricular tachycardia when the cardiac rate is 170 beats a minute. The R-R interval is absolutely constant at 370 milliseconds, and the P-R interval at 220 milliseconds.

The second strip (Figure 66b) is representative of the appearances that developed one minute after the injection of verapamil and that persisted for a total of five minutes. Ectopic atrial activity persists throughout but the rate is now 150 beats a minute; the P waves remain deformed and the P-R interval at the start of each sequence of grouped beats is 200 milliseconds. In the second beat in each sequence, the P-R interval is 250 milliseconds, and in the third beat, it is 310 milliseconds. The fourth P wave in each case is blocked and the sequence then restarts, indicating second degree atrioventricular block of the Wenckebach type with a 4:3 response.

The bottom strip (Figure 66c), recorded six minutes after the completion of the injection, and just after correction of the arrhythmia, shows sinus rhythm at a rate of 95 beats a minute with a precisely regular R-R interval of 660 milliseconds. The P wave configuration is now different from that seen during the ectopic tachycardia and identical with that seen in the same lead in tracings that had been taken previously, as well as subsequently. The P-R interval is 200 milliseconds.

The response here again indicates two phenomena occurring prior to the conversion of the paroxysmal atrial tachycardia to sinus rhythm: (a) slowing of the rate of ectopic atrial discharge from 170 to 150 beats a minute, and (b) the development of atrioventricular block, in this case of the Wenckebach type. Here too the main site of therapeutic action enabling conversion to take place appears to be the atrioventricular node, where a sufficient degree of block was produced to interrupt a re-entry mechanism. At this stage the sino-atrial node was able to regain control of the heart.

Other drugs which may stop paroxysmal supraventricular tachycardia by prolonging atrioventricular conduction and thus possibly blocking re-entry include digitalis and propranolol (Damato and Lau, 1970; Editorial, 1972). In this condition, practolol - though it works - may well not do so in this way: even at high doses, it failed to produce prolongation of the P-H time whereas propranolol did (Smithen et al., 1971). Where propranolol is contra-indicated, there is added reason for using verapamil (Hills, 1970).

Verapamil does not act therapeutically as a beta-adrenergic block (Ross and Jorgensen, 1967; Brichard and Zimmerman, 1970) nor does it have a quinidine-like action (Singh and Vaughan Williams, 1972); as a calcium-ion antagonist and thus an antagonist of electro-mechanical coupling (Fleckenstein et al., 1968; Nayler and Szeto, 1972); it may belong to a novel class of antiarrhythmic agents (Singh and Vaughan Williams, 1972).

Experience with verapamil has been discussed in some detail because it appears to be an agent that, on both theoretical and practical grounds, may be of especial therapeutic benefit in paroxysmal arrhythmias associated with pre-excitation syndromes. One word of caution is essential, related to possible use in atrial fibrillation when this complicates the Wolff-Parkinson-White syndrome. As with digitalis, it may have a greater action on the normal atrioventricular nodal pathway. This is certainly the case with digitalis but the action of verapamil on anomalous tissue is not yet established. If its action is the same as digitalis, it could potentially be dangerous under these circumstances. By tending to block conduction down the normal pathways it may favour it down the anomalous pathway and increase the speed of bombardment of the ventricle and possibly potentiate the likelihood of the occurrence of ventricular fibrillation. It seems unwise therefore to use it clinically under these circumstances until such time as it has been shown to be safe and effective under experimental conditions; and facilities for defibrillation should be at hand. In one patient in whom the Wolff-Parkinson-White syndrome was complicated by atrial fibrillation, it did not slow the ventricular rate (R.A.J. Spurrell, personal communication: incidentally, this patient's conduction was type B - see Chapter 9 - and she successfully underwent surgical treatment).

Prevention

When it comes to the prevention of attacks of paroxysmal tachycardia, one should aim to suppress the atrial or ventricular premature beats that may initiate the arrhythmia; here quinidine and beta-blocking agents are useful (Coumel, 1970). More recently verapamil has worked in individual cases (Oram et al., 1971; Reckless and Gilchrist, 1971), though whether it acts by suppressing extrasystoles or by preventing re-entry has yet to be established. Even though attacks may be controllable, their continual recurrence may make the consideration of prophylactic surgery desirable. Prophylactic agents used in these patients are indicated in Section C; quinidine and practolol (perhaps by blocking atrial or ventricular extrasystoles responsible for initiating reciprocal tachycardias) were helpful.

Arrhythmias are the prime reason for concern about the pre-excitation syndromes, and the only adverse clinical features they show; their management is thus crucial in improving the prognosis of sufferers and in minimizing morbidity.

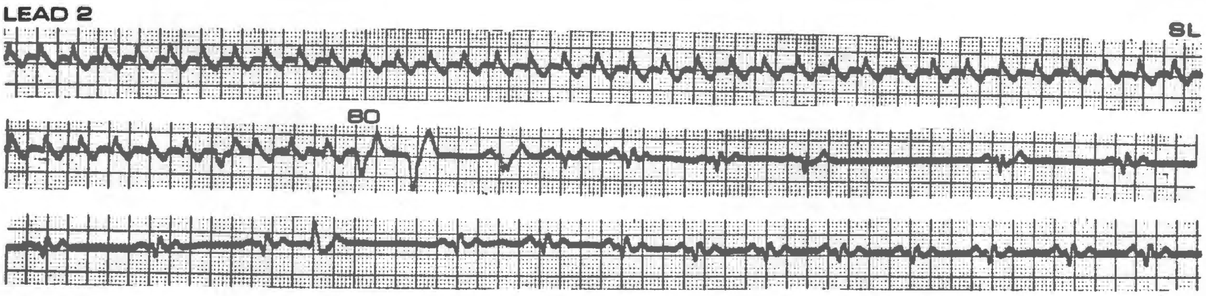


Figure 62 (Case 7) Continuous electrocardiographic strips (lead 2) after the intravenous injection of verapamil.

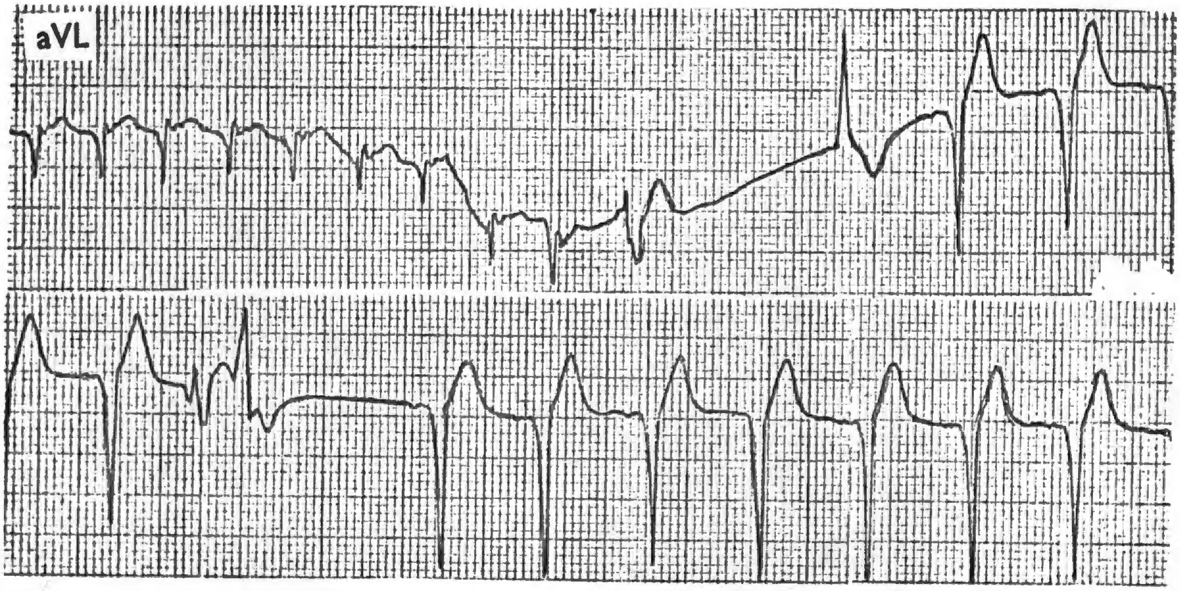


Figure 63 (Case 11) Electrocardiographic strips (continuous) showing conversion from paroxysmal tachycardia to sinus rhythm (Wolff-Parkinson-White conduction) after intravenous verapamil.

Figure 64 (Case 16) Upper strip shows atrial flutter; lower six strips recorded after intravenous injection of verapamil.

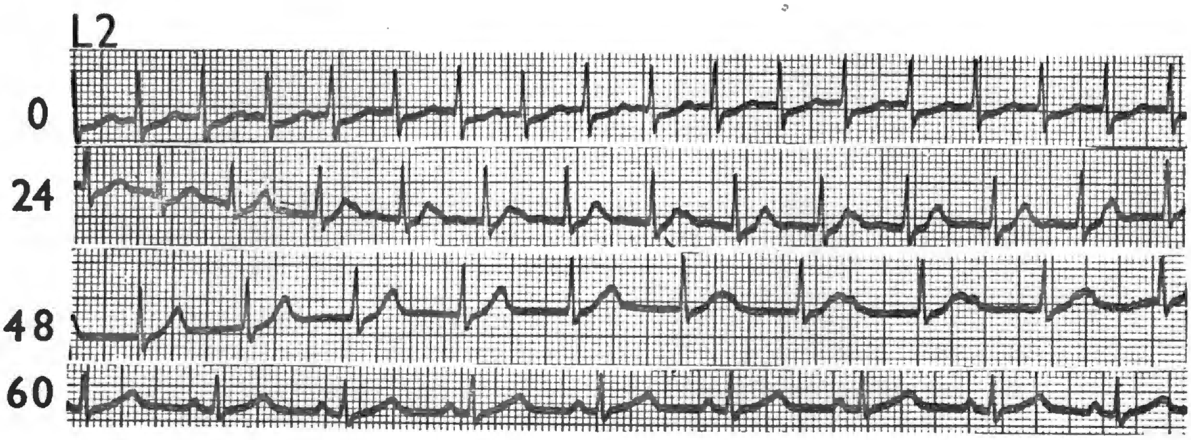


Figure 65 (Case 19) Electrocardiographic strips (lead 2) before and after administration of verapamil. 0 = control; other figures indicate number of seconds after completion of injection.

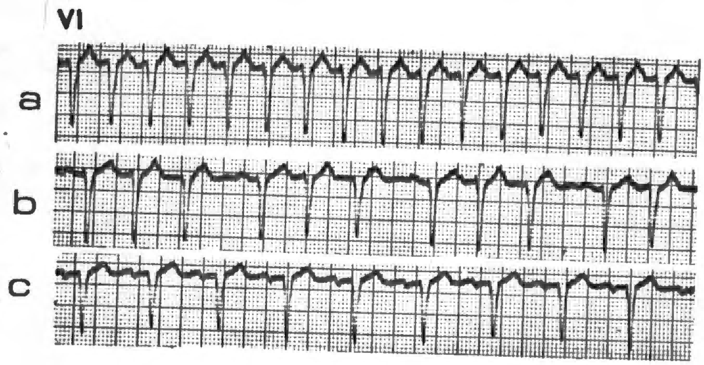


Figure 66 (Case 20) Electrocardiographic strips showing:-

(a) paroxysmal supraventricular tachycardia
(b) paroxysmal tachycardia with Wenckebach phenomenon, after intravenous verapamil;
(c) restoration to sinus rhythm after verapamil.

CHAPTER 11

"Concealed" Wolff-Parkinson-White Syndrome

In developing their theory about the role of mismatch impedance between the anomalous pathway and the ventricle it enters, De la Fuente et al. (1971) devised the animal model mentioned in Chapter 3. As they point out, the features of the model might explain some of the findings in intermittent pre-excitation. They also postulate that the structure of an anomalous pathway might be such that conduction would regularly be blocked in the atrioventricular direction, but that conduction would on the other hand occur retrogradely. This is due to the large ventricular mass able to transmit current up the "funnel" in the reverse direction, so that it reaches the atrial chamber. Thus one could have the anatomical features present that could account for the Wolff-Parkinson-White syndrome, including the occurrence of paroxysmal supraventricular tachycardia or atrial fibrillation, without ever demonstrating anomalous atrioventricular conduction. Perhaps one might qualify this by adding the phrase "during sinus rhythm or paroxysmal supraventricular tachycardia", for reasons which will become clear later. Can one thus visualize a situation in which the complicating arrhythmias associated with the Wolff-Parkinson-White syndrome may occur, yet the electrocardiogram never permits the diagnosis of the underlying disorder? If so, how could one substantiate this concept? It would of course explain the existence of anomalous pathways found on anatomical dissection, which however may never in life have produced evidence of pre-excitation. This may be the reason why Mahaim fibres - relatively common in the young (Davies, 1971) - may not have produced the electrocardiographic changes of the Wolff-Parkinson-White syndrome.

Case 14 may well fall into this category, but before considering the investigations that support this concept, two published cases merit discussion. Of the six patients with atrial fibrillation reported by Yahini et al. (1964) five had undoubted Wolff-Parkinson-White syndrome. The sixth case had bizarre and irregular delta waves during atrial fibrillation, being then indistinguishable from the other five. Many tracings taken during sinus rhythm invariably showed QRS complexes of normal configuration, and the P-R intervals were never short (J. Yahini, personal communication). The only explanation possible must depend on localized pre-excitation of a portion of ventricle away from the normal conducting tissue. Thus during atrial fibrillation impulses reach this area but not through the atrioventricular node in the normal manner. This can only be conceived as happening through an anomalous pathway of some sort. However on no occasion was this utilized anterogradely during sinus rhythm; it appears to have functioned anterogradely only during atrial fibrillation. Electrophysiological studies might prove the existence of an anomalous pathway, and should be designed to see whether retrograde ventriculoatrial conduction can occur, bypassing the atrioventricular node; and if atrial fibrillation can be induced, it should display the pattern of anomalous conduction. Apparently contact has been lost with this patient, so the hypothesis cannot be tested.

It is tempting to postulate that the case of benign atrial fibrillation reported by Levine (1963), where the condition had lasted 40 years, falls into the category of concealed or occult Wolff-Parkinson-White syndrome. This sounds like a case of lone atrial fibrillation, but the patient died suddenly following an emotional disturbance. It is plausible that this patient had an anomalous pathway, and that under normal circumstances the fibrillating atria caused no trouble because impulses from them were conducted down the atrioventricular node, and subject to its physiological delay. If during emotion the atrioventricular node was blocked and the hypothetical pathway utilized, ventricular fibrillation might have occurred as is possible in the Wolff-Parkinson-White syndrome.

It is in Case 14 that the possibility of testing the hypothesis of De la Fuente et al. (1971) arose. This patient had been admitted to hospital because of a "faint" and his electrocardiogram (Figure 67) showed sinus rhythm and a P-R interval of 0.12 seconds, with peaked P waves in leads II and aVF, but no other abnormalities. The QRS interval was 0.06 seconds, and the T wave was inverted in lead III and flattened in aVF. S-V5 + R-V2 totalled 37 mm., approximating the margin for the diagnosis of mild left ventricular hypertrophy.

When, 8 days later, he became unconscious in the presence of medical staff, ventricular fibrillation was diagnosed (Figure 68a). Immediate cardioversion restored sinus rhythm, but there was no ventricular response (Figure 68b): note the single atrial extrasystole. Atrial fibrillation developed following an early atrial extrasystole (Figure 68c); the ventricular rate increased, with ventricular extrasystoles and a short run of ventricular tachycardia (Figure 68d) and transient idioventricular tachycardia (Figure 68e): the QRS complexes became narrow (Figure 68b), and 30 minutes after the attack, sinus rhythm returned (Figure 68g). (Two hours later the T waves were upright).

Because of the borderline P-R interval, which was confirmed on other tracings, the Lown-Ganong-Levine syndrome was considered. However it was appreciated that, for reasons discussed in Chapter 9, there was no reason to anticipate that this should be complicated by ventricular fibrillation (unlike the case in the Wolff-Parkinson-White syndrome). His bundle electrography was carried out. At the resting rate (60 beats a minute), the P-H and H-Q intervals were both normal (Table XV). The appearances are shown

Table XV

Case 14: His bundle electrography

Heart rate beats/minute	P-H interval milliseconds	H-Q interval milliseconds
60	115	53
* 82	145	45
* 100	175	45
* 120	215	40
* 136	275	42

* = paced rate from high right atrial stimulation

in Figure 69, but in addition, the first and fourth complexes shown are followed by retrograde spikes, at a Q-P' interval of 140 milliseconds.

With atrial pacing, there was a physiological increase in the P-H interval from rates of 82 up to 136 beats a minute. These changes are also shown in Table XV. At pacing rates of 150 beats a minute, the H-Q interval remained quite stable at 40 milliseconds but now a Wenckebach phenomenon was apparent with a P-H interval of 190 milliseconds followed by one of 295 milliseconds, followed by a dropped beat, and a succeeding P-H interval of 177 milliseconds. Thus, the P-H and H-Q intervals were normal, and the behaviour of the P-H interval on pacing was physiological. There would therefore seem little basis for supporting the clinical suspicion of the Lown-Ganong-Levine syndrome (on the basis of a somewhat short P-R interval, and a tendency to paroxysmal arrhythmia), save that similar cases were included by Mandel et al. (1971), with similar behaviour on pacing. If this is acceptable, it must indicate that an atrioventricular nodal bypass was not operative during the particular study conducted, but that at this time the normal pathways were being utilized.

Castillo and Castellanos (1971) have shown retrograde activation of the bundle of His during His bundle electrography following the induction of ectopic ventricular beats. This does not appear to be the explanation of the deflections seen following some of the normal complexes in Figure 69, which more closely resemble atrial depolarization deflections. As can be seen from Figure 70, taken on a different occasion, some ventricular extrasystoles were followed by retrograde P waves, deforming the T waves, at an R-P' interval of 140 milliseconds. This is the same period of time as seen in the His bundle electrogram (Figure 69) and strongly supports the impression that these are indeed retrograde P waves. The importance of this observation lies in the fact that there was no retrograde H deflection between the V and P'. As pointed out by Castellanos et al. (1972), in synthesizing previous studies, ventricular beats with retrograde propagation into the atria show a His deflection sandwiched between the ventricular and low right atrial electrograms.

Referring to Case 5, it can be seen from Figure 51 that his reciprocal rhythm showed no retrograde H deflection. The postulated explanation for the absence of a retrograde H deflection in Case 14 is thus that the atria were activated by an impulse passing up an anomalous tract. This seems more likely than retrograde atrial depolarization due to return from within the atrioventricular node: functional intranodal dissociation (Mendez and Moe, 1966). Furthermore it provides the basis for the occurrence of ventricular fibrillation, by early return of the impulse into the atrial chamber, with consequent atrial fibrillation (Schamroth and Krikler, 1967b). The development of functional second-degree atrioventricular block because of concealed conduction in the atrioventricular node produced by the stimuli from the fibrillating atria may have enabled a greater amount of the conduction to pass down the hypothetical anomalous pathway. Without the interposition of the protection of the atrioventricular node during anterograde conduction, the ventricles would then be subjected to incessant bombardment along the anomalous pathway, and fibrillation could thus be induced in them.

An analogy can be made with the dog with the Wolff-Parkinson-White syndrome studied by Boineau and Moore (1970), in which ventricular fibrillation could regularly be produced following the induction of atrial fibrillation on three occasions, during intra-ventricular studies. This implies retrograde conduction into the atria via the bundle of His, which, finding the atria out of phase, sets up atrial fibrillation; then the rapid conduction of irregular atrial impulses down the bundle of Kent (anatomically demonstrated in this dog) produced ventricular fibrillation. Such a situation would of course be promoted if the P-R interval, representing anterograde conduction down the atrioventricular node, were prolonged more than usual, thus enabling re-entry to occur retrogradely into it (Goldreyer and Damato, 1970; Schamroth and Yoshonis, 1970). A similar process to that described by Dreifus et al. (1971a) can thus be envisaged, and it is likely that this also occurred in Case 14. Indeed, some cases of unexplained ventricular fibrillation may arise on this account rather than reflect the occurrence of myocardial infarction. Such patients normally die suddenly, and with the usual type of post mortem examination, in which the heart is not carefully examined for evidence of anomalous pathways, cardiac infarction would be the inescapable diagnosis to be made by the coroner. The fortuitous occurrence of the arrhythmia while he was in hospital, and the prompt availability of resuscitative measures, were the only circumstances whereby a patient like Case 14 could have survived.

The terms "concealed Wolff-Parkinson-White syndrome" or "occult Wolff-Parkinson-White syndrome" are proposed for this state of affairs. Öhnell (1944) has already used "concealed pre-excitation" for cases showing a high degree of pseudo-normalization, and we are specifically concerned with a possible bypass connected directly to the ventricle, so the Wolff-Parkinson-White label is helpful. More decisive proof is desirable, but this seems to be a realistic concept that explains certain isolated cases not otherwise easily understood.

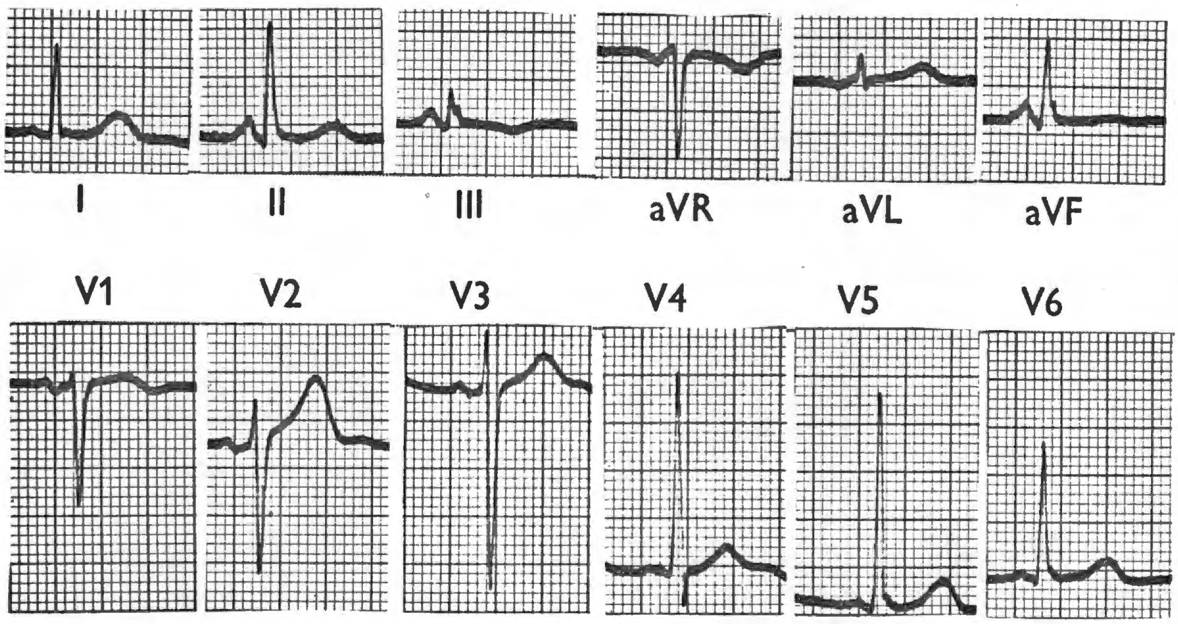


Figure 67 (Case 14) Electrocardiogram.

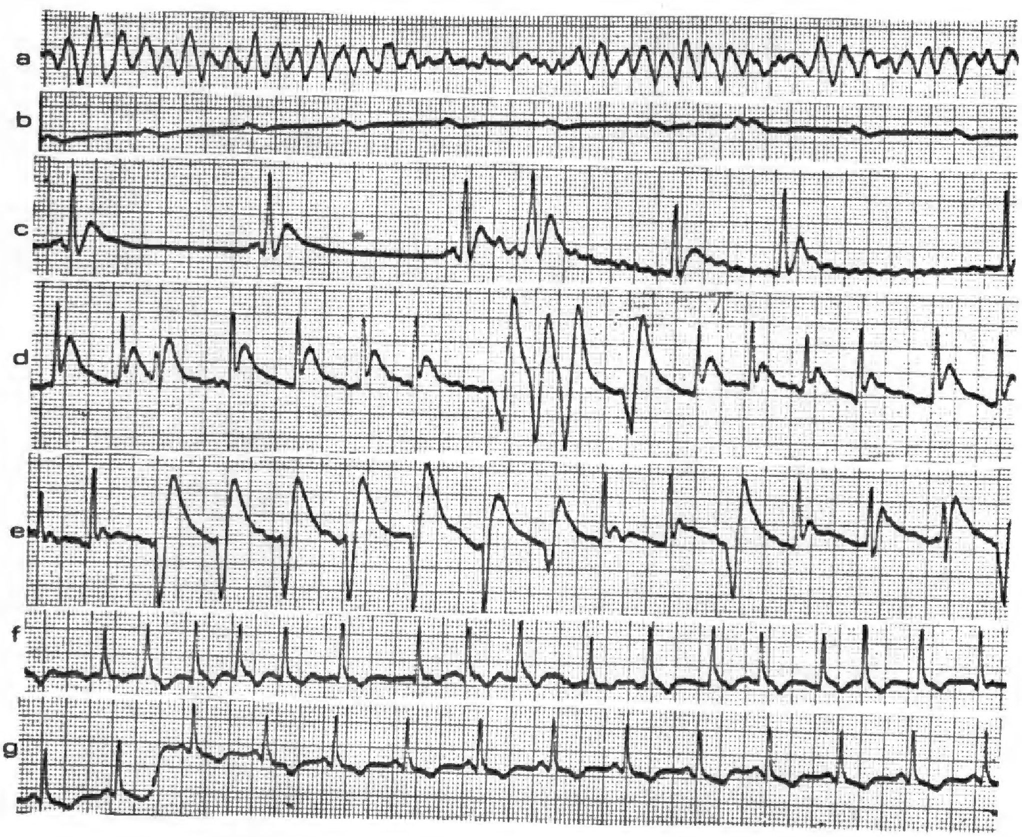


Figure 68 (Case 14) Electrocardiographic strips (lead 2) during ventricular fibrillation (a) and after defibrillation; for discussion see text.

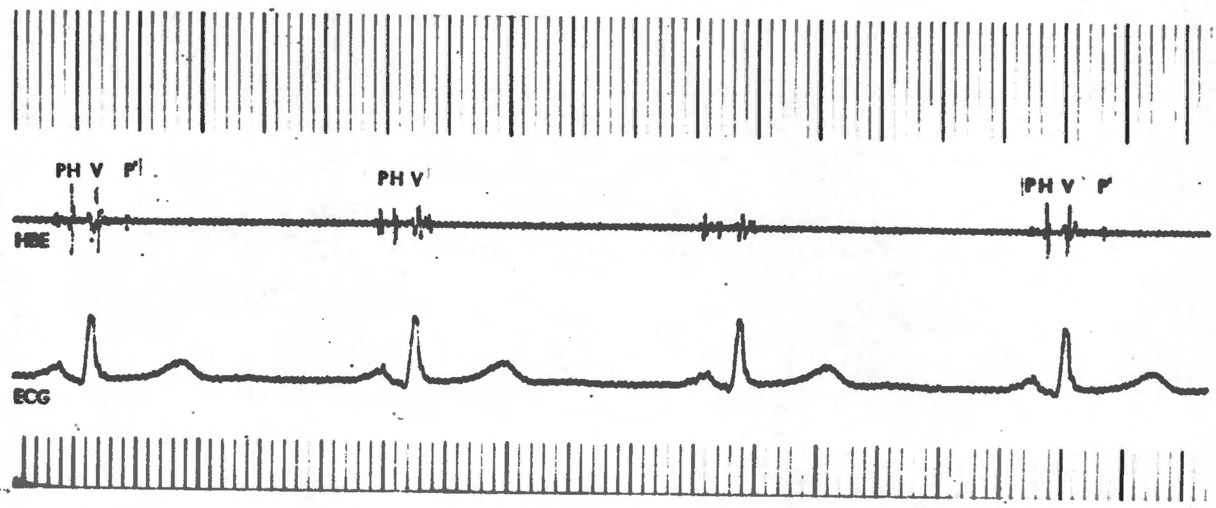


Figure 69 . (Case 14) Simultaneous His bundle electrogram and electrocardiogram.

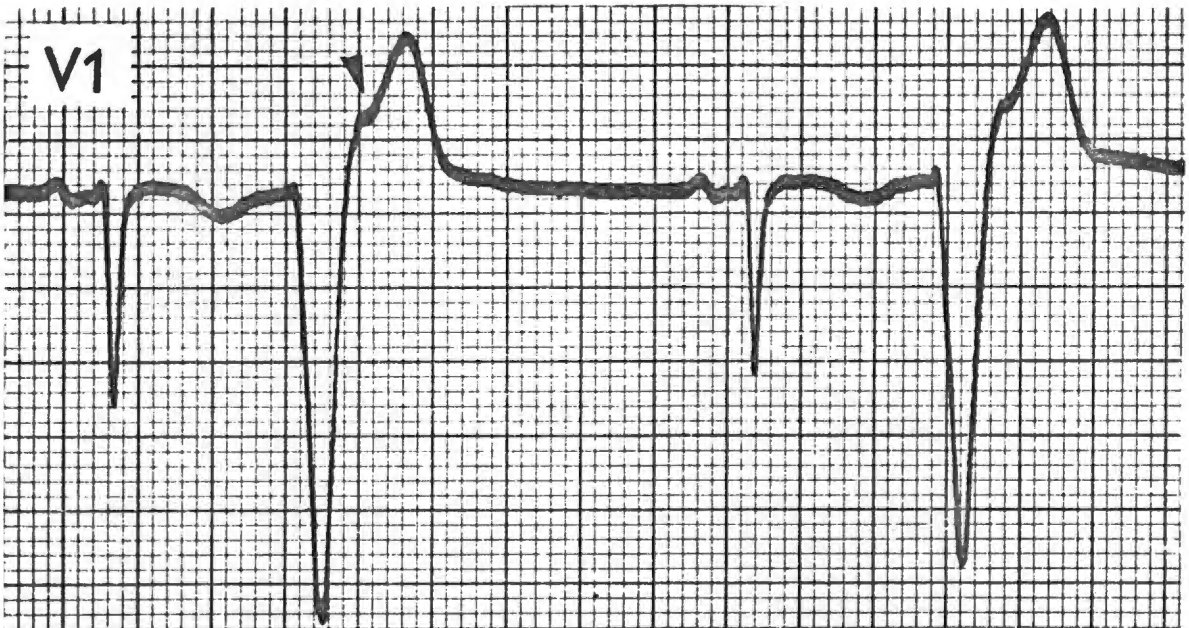


Figure 70 (Case 14) Electrocardiographic strip (V1) showing ventricular extrasystoles with retrograde P' waves.

CHAPTER 12

Apparently-acquired Wolff-Parkinson-White Syndrome

There has long been dispute as to whether or not the Wolff-Parkinson-White syndrome may be "acquired": a difficult decision to resolve in a condition which can be intermittent - indeed, in which variation in the electrocardiographic appearances can be induced in so many cases, and where normalization so often occurs spontaneously. Thus the demonstration of normal conduction (via the atrioventricular node and bundle of His) on the first occasion that a tracing is recorded, and the occurrence of the Wolff-Parkinson-White pattern subsequently, provides no basis for such an assertion.

Among disorders said to produce "acquired" Wolff-Parkinson-White syndrome are cardiac infarction (Prinzmetal et al., 1952), myocarditis (Swiderski et al., 1962) and cardiomyopathy (Braunwald et al., 1960). At once it must be stressed that the question of simulation of (or resemblance to) the Wolff-Parkinson-White syndrome by these disorders is another problem (see Section B). Although there were no previous electrocardiograms in Case 13, the features warrant discussion of the possibility of his having "acquired" Wolff-Parkinson-White syndrome due to myocarditis.

As will be shown in Section C, he presented with an acute fatal cardiac illness, and was found to have acute myocarditis and no genuine anomalous pathway.

Only one electrocardiogram was recorded and is displayed in Figures 71 and 72. No atrial activity can be seen (with the possible exception of the first complexes of lead III in Figure 71), i.e. there is third-degree sinoatrial block during almost the whole - if not the whole - of these tracings. The QRS complexes in all leads - with exceptions now to be detailed - are made up exclusively of delta waves at the rate of 40 beats a minute. The exceptions consist of ventricular escape beats, being, in Figure 71, the last complex in V1, the last two complexes in V4, the last complex in V5, and the fourth, fifth and sixth complexes in V6; the fourth and sixth complexes in V6 have slurring of their R waves and probably represent fusion between the ventricular escape beats and the delta waves.

Figure 72 consists of separate strips of V5 and V6, each lead being continuous. Again, the basic rhythm consists of isolated delta waves, with, in V5, ventricular escape beats (fourth and fifth complexes) and fusion beats (sixth and eighth): the delta wave alters its form in the seventh beat, and the ninth beat is discrepant and insufficiently well seen to bear analysis, though in these cases a varying contribution from a ventricular focus is possible. In V6, the second QRS is an escape, and the fourth shows fusion; the third shows more resemblance to its preceding (escape) beat; all the rest are delta waves. The idioventricular focus, when active, displays a rate of 50 beats a minute.

The discrepant complexes in lead III (Figure 71) appear to show P waves at the same rate, preceding ventricular activation, but with fusion in the third complex: the last three complexes, so closely resembling those in leads II and aVF, are compatible with pure delta waves.

These changes would suggest localized pre-excitation from a focus within the bypass, causing focal ventricular depolarization. Only one brief spell of possible atrial activity could be seen. At times there was brief activity from an idioventricular focus, at a slightly faster rate than the focus within the bypass (50, as opposed to 40, beats a minute), with occasional fusion between them.

The hypothesis that a latent and incomplete by-pass was activated because of inflammation between it and the interventricular septum, or because the inflammation in the myocardium decreased its effective resistance sufficiently to dissipate the mismatch impedance between these structures, will receive further consideration.

One possible mechanism for the occurrence of the Wolff-Parkinson-White syndrome in this case, the presence of anomalous pathways - appears firmly excluded by the careful dissection and histological examination of the heart, although the presence of Mahaim tracts almost but not quite making contact with the interventricular septal muscle is thought-provoking and will be discussed below. Certainly, there was no well-defined bundle of Kent, and the fact that the Mahaim fibres failed to reach the interventricular septum indicates that they, in their own right alone, could not have been responsible for the appearances of pre-excitation.

In acquired cases, it has been postulated by Sherf and James (1969) that structural blocking of the anterior and middle internodal tracts would force the sinus impulse to descend in the posterior tract and bypass the atrioventricular node. Against this explanation in this case is the fact that there was no sinoatrial activity; indeed, all that is demonstrated (Figures 71 and 72) is independent depolarization with occasional runs of fusion beats resembling the appearances of the Wolff-Parkinson-White syndrome, i.e. a focus within the presumed "bypass" area, at times causing local depolarization, and at times more completely activating the ventricles. This fits in with the other suggestion by Sherf and James (1969) that under these circumstances there might be appropriately located ectopic pacemaking activity.

The suggestion that an excitable centre in the ventricle may explain the abnormal QRS complexes of the Wolff-Parkinson-White syndrome was raised by Holzmann and Scherf (1932); the mechanical effect of a sinus-induced atrial contraction might prematurely cause ventricular contraction; but if this were to lead to paroxysmal tachycardia it should then be ventricular, and we know that this is rarely - probably never - the type of arrhythmia seen (Scherf and Cohen, 1964). However the latter workers did not exclude the possible presence of an excitable centre in "acquired pre-excitation", e.g. myocarditis; and the findings in Case 13 would be compatible with this. Indeed, no atrial mechanical activation of such a centre need - or indeed can - be invoked here, for the electrocardiographic pattern appeared to be entirely ventricular in origin, whether due to sinoventricular conduction, complete sinoatrial block or sinus arrest.

The inflammatory reaction within the myocardium and the conducting tissue was sufficiently intense to suggest the possibility that it alone is responsible. There were, however, no signs of extrasystoles arising elsewhere in the heart, and it seems more logical to pursue the question as to why the ectopic pacemaking activity arose where it did. The lack of previous electrocardiograms in this patient made it impossible to see what sort of change had taken place from the basic situation. One assumes that the intensity of the inflammation was sufficient to suppress sinoatrial activity, and that the subsidiary pacemaking centre that took over produced the predominantly-

localized depolarization seen in these tracings.
It is difficult to draw conclusions with regard to the case of myocarditis as described by Swiderski et al. (1962) as their patient survived. Evidence of the Wolff-Parkinson-White syndrome was only seen during the myocarditis, and never since. The present case however, has clear pathological proof that there was inflammation of the myocardium. Possibly one can relate the findings in Case 13 to the concept of dissipation of impedance mismatch. Conduction of impulses down the fasciculi seen would not normally reach the interventricular septum, and thus produce pre-excitation, because of lack of anatomical continuity. Indeed, in their own right, these fasciculi were not considered by Professor R.E.B. Hudson or by Dr. E.G.J. Olsen to be of any particular significance. However, with inflammation within these fasciculi, it would be possible for an impulse to be generated; and if the inflammatory infiltration between the fasciculi and the myocardium were thereby rendered conductive, it would be possible for impulses to cross from them into the heart muscle proper and for depolarization to occur. At times the relatively

small input current from the fasciculi would be drained off by neighbouring cells, dissipated, and thus lead to no more than the registration of the delta waves due to localized pre-excitation; at other times, with conduction extending more generally into the myocardium, there would be fusion between delta wave and ventricular activation, with inscription of the Wolff-Parkinson-White complexes seen.

It is not postulated that this is a fundamental mechanism for the occurrence of the Wolff-Parkinson-White syndrome, but rather that, where the genuine syndrome occurs in the presence of myocarditis or cardiomyopathy, such a mechanism might be temporarily operative. It might for example explain the features described in their case by Swiderski et al. (1962). An explanation of this sort seems at least as likely as that suggested by Sherf and James (1969). The obvious failure of impulse generation and conduction through the normal pathways would favour an increased input into the rudimentary anomalous pathway, as suggested by Schamroth (1971a).

One other factor that, theoretically, may help dissipate the mismatch impedance and enable current to traverse the bypass, would be a decrease in ventricular myocardial potential. This phenomenon has been shown to occur in acute cardiac infarction (Chatterjee et al., 1971) and in acute massive pulmonary embolism (Chatterjee et al., 1972). It is conceivable that changes of this nature occurring in those with bypasses in whom antegrade conduction is inapparent, may have this brought to light under such circumstances. Furthermore, this raises the possibility of the occurrence of a similar phenomenon in cardiomyopathy and myocarditis, though this does not yet appear to have been investigated. It may have been a factor favouring anomalous conduction in Case 13, the intense myocardial inflammation possibly having decreased the myocardial potential.

The production of the Wolff-Parkinson-White syndrome in disorders of cardiac muscle may therefore be more easily induced when the substrate - an anomalous bypass not normally functioning - exists; or when, as in Case 13, it is rudimentary. Factors producing imtermittent Wolff-Parkinson-White syndrome may do so, therefore, because their blocking effect on the normal atrioventricular nodal pathways may thus tend to favour entry of a larger current into the filament that makes up the anomalous pathway. As Schamroth (1971a) indicates, "the so-called acquired form of Wolff-Parkinson-White syndrome may merely be an unmasking of a latent Wolff-Parkinson-White syndrome".

It is suggested that this concept be expanded, and that factors that decrease ventricular myocardial potential as well as those acting directly on the atrioventricular node and on occult or incomplete anomalous pathwaysmay produce apparently acquired pre-excitation. Herein may be found the explanation for the apparent development of the Wolff-Parkinson-White syndrome in myocarditis, cardiomyopathy and cardiac infarction. These latter disorders may reveal the substrate, hidden and inactive until so brought to light. This might be looked upon as "revealed" rather than "acquired" Wolff-Parkinson-White syndrome. That some cases of "concealed Wolff-Parkinson-White syndrome" may present in this way, instead of by virtue of the arrhythmias that may occur on the basis of the mechanisms postulated in Chapter 11, bears consideration.

An interesting question posed by the experience with Case 13 is what would have happened had he survived? He might of course have had evident Wolff-Parkinson-White conduction previously, but we have no proof of this; and the anatomical evidence does not suggest that this was probable. If his myocarditis was of viral origin, it might have gone on to cardiomyopathy (Burch and Giles, 1972), and one can only conjecture whether or not the severity of resultant muscle disease might have lowered ventricular "resistance" and favoured persistent anomalous conduction.

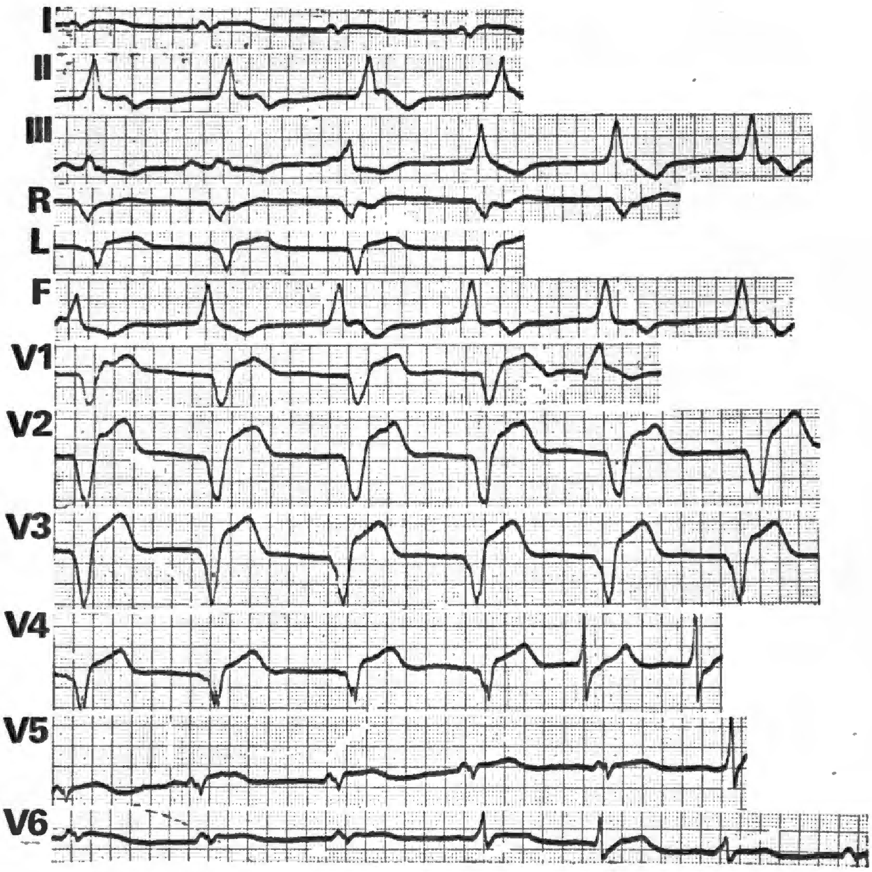


Figure 71 (Case 13) Electrocardiogram

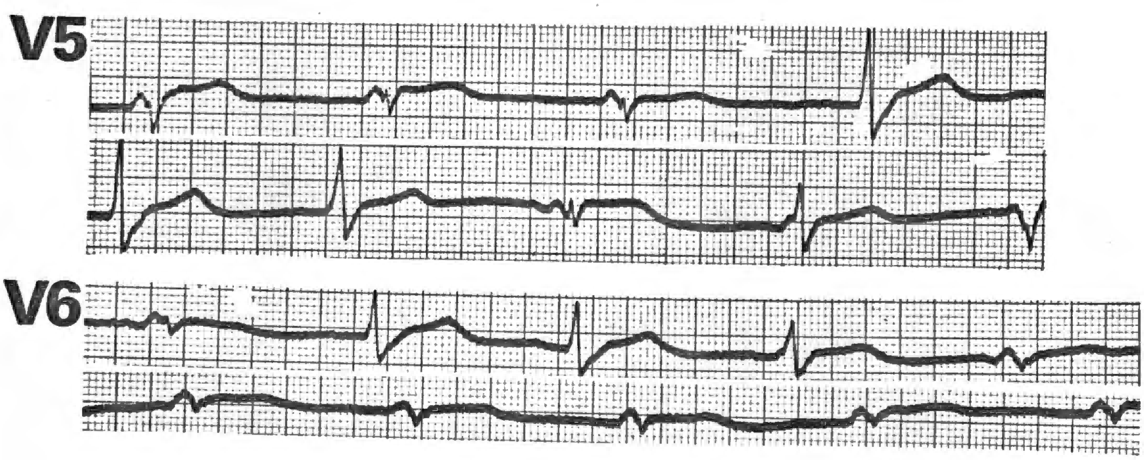


Figure 72 (Case 13) Electrocardiographic strips, V5 and V6 (each lead is continuous).

SECTION B

CONDITIONS THAT MAY RESEMBLE OR MIMIC PRE-EXCITATION

CHAPTER 13

Cardiomyopathies

In Chapter 12, a possible mechanism whereby cardiomyopathy might be causally responsible for the Wolff-Parkinson-White syndrome was discussed. On the other hand, cardiomyopathy may produce electrocardiographic appearances resembling or indeed at times simulating the Wolff-Parkinson-White syndrome. Both situations may indeed co-exist: and at times chance might determine the fortuitous occurrence of the Wolff-Parkinson-White syndrome and a cardiomyopathy.

It has been noted that an electrocardiographic pattern resembling the Wolff-Parkinson-White syndrome is not uncommon in hypertrophic obstructive cardiomyopathy (Editorial, 1966) and a possible association between the syndromes has been reviewed by Braunwald et al. (1964). In their own series of 64 cases, they found a classical pattern in 2 cases, and publish tracings from one patient showing, on one occasion, the typical appearances of the Wolff-Parkinson-White syndrome, type B, and on another occasion, 10 months later, changes consistent with mild left ventricular hypertrophy without any evidence of pre-excitation. However, another two patients might well have the Wolff-Parkinson-White syndrome, for they had shortening of the P-R interval with what was considered to be a delta wave (slurring of the start of the R wave) but with a normal QRS duration. A further 21 patients had only a delta wave, with no P-R shortening or QRS prolongation. They commented that the 27 cases with a delta wave tended to have significantly greater left ventricular outflow obstruction (average gradient 80 mm. Hg) than the 37 patients without a delta wave (average gradient 41 mm. Hg) ($P < 0.01$).

Here one should also note their finding that in hypertrophic obstructive cardiomyopathy, abnormally deep and broad Q waves, not however indicative of cardiac infarction, tended to occur (in 16 of their 64 cases) and that these Q waves were more common in those with familial cardiomyopathy (10 of 23 cases, 44%) than in non-familial cases (6 of 41 cases, 15%) ($P < 0.02$). A number of patients with hypertrophic obstructive cardiomyopathy reported by Prescott et al. (1963) also had abnormal Q waves simulating cardiac infarction.

Braunwald et al. (1964) did not discuss the occurrence of arrhythmias in their cases and thus did not show (nor postulate) the mechanism of arrhythmias, and the fate of the "delta" wave when the origin of the rhythm moved from the sinoatrial node; nor did they discuss (other than by implying a possible relationship to the severity of the subaortic obstruction) how such a delta wave might be produced. As regards the pathological Q waves, these were correlated with septal hypertrophy due to depolarization of the hypertrophied interventricular septum, and possibly in part to patchy myocardial fibrosis.

The main changes in cardiomyopathy that might cause confusion with pre-excitation will thus be related to the occurrence singly or in combination of P-R shortening, slurring of the commencement of the R waves (with or without QRS widening) and arrhythmias. Before considering these aspects in various patients, a comment will be made on the possible pathogenesis of some of the appearances. A useful starting point for this is the report by Harmjanz et al. (1971) of an analysis of 25 patients with hypertrophic obstructive cardiomyopathy in whom they performed apex cardiography, electrocardiography, and left and right heart catheterization: in 13, biplane angiocardiograms were performed, within an interval of a few minutes, of both ventricles. Pathological Q waves were found in leads V3 - V7 in 10 cases; delta waves were found in V4 - V7 in 6 patients and in other leads in a further 5 cases. Those cases who exhibited pathological Q waves in chest leads had only a slight prolongation of the isovolumetric relaxation period (as judged by apex cardiography): here the angiocardiogram revealed local hypertrophy of the ventricular septum. In contrast, the patients with delta waves in V4 - V7 showed marked prolongation of the isovolumetric relaxation period, and on angiocardiography the ventricular septum was diffusely (as opposed to focally) hypertrophied. They considered these Q and delta waves to indicate early septal activation, and showed that these deflections preceded the R waves of other leads instead of occurring coincidentally, as is normal in all chest leads.

Harmjanz et al. (1971) thus postulate the formation of a localized area of ventricular pre-excitation by the pathological process in hypertrophic obstructive cardiomyopathy. In the true Wolff-Parkinson-White syndrome, of course, the first deflection of the QRS complex occurs synchronously in all chest leads, unlike the case here; though their one patient with delta waves in all chest leads, with widely diffuse ventricular hypertrophy, more closely resembled the true Wolff-Parkinson-White syndrome. This theory is in keeping with the finding of unduly early activation of the anterior paraseptal basal region of the heart (in advance of the apical region, instead of, as normal, after it) as found in hypertrophic obstructive cardiomyopathy by Snellen (1964).

Durrer (1968) has also considered the genesis of the abnormally deep and broad Q waves found in left precordial leads in some patients with cardiomyopathy. One possible explanation (for which he did not find support in a single case in whom he explored septal excitation) is an increase in the area supplied by the left bundle (because of an increase in the muscle bulk) - this would theoretically conform with the occurrence of localized pre-excitation because of mismatch impedance. Another explanation could be that the voltage generated by the septal forces is larger than normal; he was unable to find any direct evidence to support this hypothesis. He favours a third hypothesis, on the basis of the study of a patient with hypertrophic obstructive cardiomyopathy; much of the excitation of the ventricular wall appeared to occur synchronously instead of, as normal, in an outward direction; thus there is nearly complete cancellation of these excitatory forces, resulting in a broad epicardial Q wave. Only one of the 25 cases reported by Harmjanz et al. (1971) had a slightly short P-R interval (0.12 seconds) and this case did not have a delta wave; it exceeded this value in the remaining 24, and in only one of these (with left bundle branch block and a QRS of 0.15 seconds) did the QRS exceed 0.12 seconds. One can thus confirm the assertion of these workers that in some respects their tracings resembled - but did not present as - the Wolff-Parkinson-White syndrome. No arrhythmias occurred; thus again, the behaviour of the delta wave during a rhythm disturbance could not be assessed.

How might this local pre-excitation occur, and how might it be related and compared to the Wolff-Parkinson-White syndrome more generally? Here we touch on electrophysiology, anatomy and genetics.

As has been indicated elsewhere, the manifestation (or unmasking) of the Wolff-Parkinson-White syndrome on the one hand, and its suppression, on the other, may be related to the phenomenon of mismatch impedance (Mendez et al., 1970; Schamroth, 1971a). While the production of interference with anterograde conduction down the atrioventricular node could enhance the importance of a latent pathway, this is not to be expected in a disorder of cardiac muscle. Three possibilities arise if the Wolff-Parkinson-White syndrome is to occur in hypertrophic obstructive cardiomyopathy (or other primary disease of heart muscle):

(a) enhancement of conduction down a latent anomalous pathway;

(b) fortuitous delimitation by inflammatory tissue of a bypass, through normal cells, conducting supraventricular impulses into the ventricular chamber;

(c) the production of an excitable area within or close to the normal anatomical conducting pathways (as has been postulated for the Wolff-

Parkinson-White syndrome and previously discussed).

In the case of paroxysmal tachycardia under such circumstances, the behaviour of the delta waves during the arrhythmia may provide a valuable indication as to whether or not the mechanism is reciprocal or extraystolic. Consideration of Cases 21 and 22 will enable these aspects to be further explored.

Case 21

On admission the electrocardiogram showed regular atrial activation at the rate of 240 beats a minute, with a ventricular rate of 120; the QRS interval was 0.12 seconds, and there were tall R waves in leads I, aVL and V6, with deep S waves in V1 (Figure 73a). The diagnosis of paroxysmal atrial tachycardia (or flutter) with 2:1 atrioventricular block was made and the patient was given 10 mg. of verapamil intravenously, with prompt conversion to atrial fibrillation (Figure 73b). This in turn was treated with direct current cardioversion (using 100 joules), with an immediate return to sinus rhythm.

In sinus rhythm (heart rate 50 beats a minute) a tracing when the patient had been off all treatment for three days (Figure 74), shows a P-R interval of 0.20 seconds, and QRS complex 0.10 seconds in duration. Tall R waves are evident in leads I, aVL and V6, with deep S waves in V1; and the tall R waves in the relevant leads are to varying degrees deformed by initial slurring. The QRS configuration remains identical irrespective of the rhythm, whether supraventricular tachycardia or atrial flutter, atrial fibrillation, or sinus rhythm. The persistence of the heavily-slurred R waves ("pseudo-delta") is well seen in both paroxysmal supraventricular tachycardia and in atrial fibrillation (Figure 75); panel (a) shows paroxysmal tachycardia (150 beats a minute), with 1:1 conduction, and panel (b) atrial fibrillation (ventricular rate approximately 110 beats a minute).

As discussed in Chapter 8, it is the general rule in the paroxysmal tachycardia of the Wolff-Parkinson-White syndrome for anterograde conduction to traverse the bundle of His, with consequent normalization of the previous electrocardiographic appearances seen in sinus rhythm. Furthermore, a reciprocating mechanism involves 1:1 conduction at some stage in the process, and the 2:1 response seen in Figure 73a will not permit this to continue, unless the 2:1 response was confined to the final common path. However if there were an anomalous pathway producing a delta wave, this should have disappeared during the tachycardia unless it utilized a bypass anterogradely - but the response is more characteristic of the behaviour of the atrioventricular node. Whether this arrhythmia is called paroxysmal atrial tachycardia or flutter is more of semantic than practical importance; apart from the rate, which is on the fast side for this diagnosis, tachycardia seems to fit best. It is possible that the failure of the paroxysmal tachycardia to change to sinus rhythm with verapamil partly reflects the fact that there was no re-entry mechanism operative in this arrhythmia.

The situation in Case 21 was then investigated with His bundle electrography. In sinus rhythm (heart rate 65 beats a minute) the P-H and H-Q intervals were normal (Figure 76), and with atrial pacing the P-H interval lengthened but the H-Q interval remained unchanged (Figures 77 and 78): see Table XVI. These studies thus showed no evidence of any

Table XVI

His bundle electrogram, Case 21

Heart Rate beats/minute	Cycle length R-R milliseconds	P-H interval milliseconds	H-Q interval milliseconds
65	935	165	40
* 148	430	220	40
* 158	380	230	40

* paced from high right atrium

pathways bypassing the atrioventricular node, as the H-Q interval was normal during sinus rhythm and did not become shorter during atrial pacing. Furthermore, the P-H interval was well within the normal range at rest and showed the type of prolongation encountered normally when the heart rate is increased by means of atrial pacing.

Case 22

Five tracings recorded during his stay in hospital showed the features present in Figure 79. The rhythm is atrial fibrillation and the ventricular rate 60 beats a minute. The mean manifest frontal plane axis of QRS is -25°; QRS interval 0.08 seconds. The R waves in leads I and aVL are deformed at their commencement by slurring-notching (like delta waves), and there are minute Q waves in II, III and aVF. The sum of R-V5 and S-V2 is 65 mm., and there are inverted T waves in I, aVL and V4-6, indicating marked left ventricular hypertrophy.

Here, too, during atrial fibrillation there are basically normal QRS complexes, albeit modified by severe left ventricular hypertrophy; as in Case 21, and unlike Case 7 - who has the Wolff-Parkinson-White syndrome - the occurrence of atrial fibrillation did not lead to exclusive or predominant delta waves.

Case 23

Figure 80 is representative of many tracings recorded over a period of a year; this one was made prior to the administration of digitalis. The patient was in sinus rhythm (84 beats a minute), with a P-R interval of 0.16 seconds; the QRS is 0.08 seconds. ST segment depression is evident in leads I, II, III, aVF and V2-6. Left ventricular hypertrophy is diagnosed on the finding that the sum of R-V4 and S-V2 is 62 mm. In addition, slurring of the upstroke of the R wave is evident in leads II, aVF and V3-6, and most noticeable, with apparent delta waves, in aVF and V3. In addition there is distortion of Q in lead III. An important point against the slurring of the R waves being due to true delta waves is the fact that there are preceding Q waves in leads II, aVF, V5 and V6; but these are not so prominent as to suggest the presence of cardiac infarction, whether true or mimicked by cardiomyopathy.

When the patient developed atrial fibrillation, the QRS complexes were similar to those seen in sinus rhythm, as was the situation in Cases 21 and 22. She received verapamil (10 mg. by rapid intravenous injection) and the response can be seen in Figure 81. Atrial fibrillation with an irregular ventricular response can be seen in the top two strips; there was then regularization of the ventricular response (seen in the bottom three strips); the amplitude of the fibrillatory (f) waves was decreased (bottom strip). These changes are typical of the response in atrial fibrillation (Schamroth, 1971b; Schamroth et al., 1972). The following day the rhythm converted spontaneously to sinus rhythm.

Because of the report by Braunwald et al. (1960; 1964) and of others cited below, and because of the features discussed in Cases 21, 22 and 23 - and the similarities to and differences from findings in the Wolff-Parkinson-White syndrome, it was decided to analyse tracings from other patients with cardiomyopathies. Accordingly, the clinical records and electrocardiograms of 52 cases with cardiomyopathy were examined in order to assess the occurrence of the Wolff-Parkinson-White syndrome or of features resembling it.

In all cases the diagnostic criteria of Goodwin (1970) were met; there were 48 patients with hypertrophic obstructive cardiomyopathy and 4 with congestive cardiomyopathy. In 31 cases (all hypertrophic) there were no electrocardiographic signs to suggest pre-excitation. Two cases of hypertrophic obstructive cardiomyopathy had unequivocal evidence of the Wolff-Parkinson-White syndrome, in each in one of two available tracings, as shown in Table XVII.

The inbetween, atypical cases, totalled 19, and included, inter alia, the following examples:

(a) One patient in whom the P-R interval was 0.22 seconds, and the QRS 0.16 seconds, with prominent delta waves (only limb leads available); atrial flutter subsequently developed.

(b) Two cases in whom the P-R interval was 0.12 seconds, the QRS 0.08-0.10 seconds, and R waves slurred.

(c) One patient with atrial fibrillation; QRS 0.14 seconds, and slurred R waves (only limb leads available).

(d) One patient with atrial fibrillation, and normal QRS complexes (0.08 seconds).

Table XVII

Electrocardiographic features in two patients with cardiomyopathy, during anomalous and during normal conduction

		P-R interval	QRS complex	Features
(a)	During pre-excitation	0.12 seconds	0.12 seconds	Type B
	Normal conduction	0.14 seconds	0.08 seconds	Minor R slurring; left ventricular hypertrophy
(b)	During pre-excitation	0.10 seconds	0.14 seconds	Type A
	Normal conduction	0.12 seconds	0.08 seconds	Left ventricular hypertrophy

(e) Ten cases with P-R intervals between 0.12 and 0.20 seconds, QRS 0.08-0.11 seconds, and slurring of the R waves, sometimes with manifest or apparent delta waves, e.g. Cases 21, 22 and 23, both of whom had atrial arrhythmias; and Case 24, who did not.

Of the latter group, Case 24 is interesting in that the signs of R wave slurring were variable. In most of his tracings, the appearances seen in Figure 82 were evident. This reveals sinus rhythm at the rate of 76 beats a minute, P-R interval 0.18 seconds, and QRS 0.07 seconds. The R wave in lead I is 25 mm. tall and in aVL, 18 mm.; the sum of R in V5 and S in V2 is 45 mm. In addition the ST segments are depressed in leads I, II, aVL and V6. The commencement of the R wave is slurred in leads I, aVL and V6, looking very much like a delta wave in aVL. These appearances suggest left ventricular hypertrophy with features possibly indicating the cardiomyopathy. Yet on two other occasions, electrocardiograms showed the features seen in Figure 83, which was recorded one year after Figure 82. Again, the patient was in sinus rhythm, and the signs of left ventricular hypertrophy are even more prominent, as judged by the inverted T waves in leads I, II, aVL and V3-V6. The P-R interval is unchanged, the QRS narrower (0.05 seconds), and the slight slurring of the origin of the R less evident.

Can these appearances be due to left ventricular hypertrophy alone? Certainly, it is common in patients who do have left ventricular hypertrophy for the R wave to commence its rise gradually. This is rarely as definite as seen in the cases of cardiomyopathy now described. In none of the 50 patients with hypertension listed in Table X was such a rise more than gradual, and it did not resemble the changes herein noted. A further 46 patients with cardiac enlargement and undoubted rheumatic heart disease were therefore studied electrocardiographically. In each case the patient had either aortic incompetence, mitral incompetence, or both, with or without the addition of aortic and mitral stenosis. In only one of these patients was the electrocardiogram suggestive of this picture of a delta or pseudo-delta wave (Case 25) and here a possible explanation exists (see Chapter 14).

Of the 52 cases studied, five had documented atrial arrhythmias; and of these five, three had delta waves and two did not. On the other hand, of the 18 cases with slurred R waves (possible delta waves), only 3 had atrial arrhythmias. The importance of delta waves due to localized pre-excitation, in the genesis of arrhythmias, is not established, but if they are sought in cases of cardiomyopathy, they may be found to be prognostically important in indicating the likelihood that an arrhythmia may supervene during the course of the disorder. This does not, of course, rule out other possible mechanisms for the production of arrhythmias in primary disorders of heart muscle.

It is instructive that Cases 21, 22, 23 and 24 suffer from clinically typical congestive cardiomyopathy (and certainly show none of the features of hypertrophic obstructive cardiomyopathy); yet they have the delta waves on electrocardiography, claimed by Harmjanz et al. (1971) to be found in the hypertrophic obstructive form. This lends further weight to the comment by Goodwin (1970) when, in re-evaluating the cardiomyopathies, he found that the diagnostic distinctions between them are sometimes rather more blurred than previously supposed, though he stressed this aspect when dealing with terminal cases.

How might an area of localized pre-excitation initiate arrhythmias? Experience gained from the study of Case 13, with myocarditis, appears relevant, and was considered in Chapter 12. It is plausible that in these cases of cardiomyopathy, normally there might also, as previously suggested, be inactive pre-existent abnormal pathways, e.g. Mahaim tracts not quite - or perhaps even - reaching the interventricular musculature; but when inserted into hypertrophied or inflamed muscle, the mismatch impedance might be overcome. But, one must ask: are these initial slurred portions of R waves really delta waves? And how close is the resemblance to the Wolff-Parkinson-White syndrome? On morphological grounds, one is justified in using the term "delta wave" if one follows the criteria for the diagnosis of pre-excitation propounded by Öhnell (1944). In his type C, the P-R interval exceeds 0.12 seconds, and QRS is 0.10 seconds or less: his pure type C has a slowly-rising delta i.e. a definite slur; in C1, the QRS rises more rapidly and the delta is less easily visible as an apparently separate component. Retrospectively, however, one must now question whether, using current criteria, such were cases of true Wolff-Parkinson-White syndrome, or, as discussed below, of cardiomyopathy resembling (possibly with localized) pre-excitation.

To some extent the answer to this has been produced by Van Dam et al. (1972), who studied ten patients with proven left ventricular outflow obstruction due to hypertrophic obstructive cardiomyopathy. They investigated the time sequence of activation at the epicardial surface of the heart, in the left ventricular wall and in the interventricular septum, using epicardial exploration and intramural needle electrodes. This was carried out during surgical exposure prior to intracardiac operations on these patients. They found a variable delay of the order of 15-40 milliseconds, in subendocardial activation of the anterior paraseptal left ventricular wall, and thought that this was probably caused by a block in the anterior division of the left bundle branch. In addition, there was further retardation of epicardial excitation by the increased diameter of the left ventricular wall produced by hypertrophy, though conduction velocity in both the left ventricular wall and in the interventricular septum was roughly normal, and proceeded basically in a normal direction, i.e. from left to right. They thought that the time taken to activate the septum was prolonged because of the hypertrophy.

These workers attempted to apply the results of their work to the explanation of the precordial and epicardial Q waves sometimes present in hypertrophic obstructive cardiomyopathy. They did feel that the irregular hypertrophy found in this condition could be responsible for many abnormal initial depolarization fronts in the inner part of the left ventricular wall, creating an individually variable degree of cancellation, hence the possibility that some cases might show Q waves. Correspondingly, one might deduce that the explanation of the slurred R waves would be on a similar basis. Indeed, inspecting figure 3 of their paper, one can clearly see slurring of this sort in V4 and V5 and, in their figure 4, such changes are evident in aVL. It does seem that, quite apart from the degree of hypertrophy present, and any left ventricular outflow obstruction, uncoordinated depolarization is present in certain cases of cardiomyopathy. Judging from the experience reported in the present series of cases, this may occur in congestive cardiomyopathy as well as in the hypertrophic form. There thus appear to be two separate mechanisms that may be responsible for the slurred R waves in some leads in cardiomyopathies. On the one hand, one sees a resemblance to incomplete left bundle branch block (Schamroth and Bradlow, 1964), and here the excitation studies of Van Dam et al. (1972) provide an explanation; on the other hand, localized pre-excitation (Harmjanz et al., 1971) does appear to occur. There seems no reason why either, or the combination, might not be responsible for different appearances in different conditions. This is of course quite apart from the apparent true Wolff-Parkinson-White syndrome occurring in association with cardiomyopathy or myocarditis.

At the tissue level, an explanation for these findings - at least in hypertrophic obstructive cardiomyopathy - may be in the work of Coltart and Meldrum (1970), who recorded transmembrane action potentials of cardiac myofibrils from a patient with this disorder. They showed that the repolarization time was appreciably prolonged and that the maximum rate of follow was grossly reduced. This electrical abnormality was considered to be compatible with the late and irregular activation of the ventricular muscle in the disease. This again suggests, that if the process is patchy, normal early depolarization would be followed by delayed repolarization with simulation of pre-excitation on this account.

Of great relevance to the whole topic is the report by Massumi (1967) of familial Wolff-Parkinson-White syndrome with cardiomyopathy. This paper requires critical analysis, for the propositus has many features in common with Case 21. At the age of 14, when quite asymptomatic, a routine chest X-ray had revealed unexplained left ventricular hypertrophy. Three years later he presented with paroxysmal tachycardia, with a ventricular rate of 190 beats a minute, and an atrial rate of 380: an oesophageal electrocardiogram enabled the atrial rate and rhythm to be established. Direct current countershock converted the rhythm to normal. It can be clearly seen that the QRS configuration was identical during the tachycardia and sinus rhythm, with the "delta" wave clearly visible under both circumstances. In sinus rhythm the P-R interval was about 0.12 seconds and the QRS about 0.10

seconds. A Q wave is evident in leads I, V5 and V6 and is more marked in aVL; delta waves are difficult to discern in his figure 3. Similar changes can be seen in the electrocardiograms of the mother and one of the two siblings of the propositus, both of whom had asymptomatic left ventricular hypertrophy and similar electrocardiographic changes, but no arrhythmias.

The propositus, at the time of the report by Massumi (1967), appeared to be suffering from progressive left ventricular failure. One may take issue with the assertion that this is a family with both (true) Wolff-Parkinson-White syndrome <u>and</u> cardiomyopathy. It seems unnecessary to invoke this association (as he does) for the occurrence of left ventricular failure in his case "after only two days of tachycardia" - the ventricular rate (190) was excessively rapid, and the myocardium diseased: this could suffice to produce cardiac failure. His patient, by definition (a regular atrial rate of 380 beats a minute, and 2:1 atrioventricular block) had atrial flutter; but it seems unjustified to claim that its failure to respond to carotid sinus pressure or digitalis favoured the Wolff-Parkinson-White syndrome.

The reciprocating mechanism of the tachycardia will cease to function not only in atrial fibrillation but also in atrial flutter: indeed, while a reciprocal mechanism might be thought to be the only means whereby this could occur, just as in paroxysmal atrial tachycardia, it is the second degree anterograde block in the atrioventricular node that determines the ventricular response. Thus one would see, both in Case 21 and in case 1 of Massumi (1967), either narrow (i.e. normalized) QRS complexes during atrial flutter, as in atrial tachycardia, or even more bizarre QRS complexes due to predominant conduction down the anomalous pathway only, i.e. only delta waves rather than typical Wolff-Parkinson-White fusion beats indistinguishable from those seen during sinus rhythm.

As in Case 16, atrial flutter can occur in a patient with a pre-excitation syndrome; but its persistence cannot depend upon a continuous reciprocating mechanism (unless on the basis of 2:1 block affecting the final common pathway). Thus Massumi's case 1 does not have the typical reciprocating tachycardia of the Wolff-Parkinson-White syndrome, quite apart from the other atypical features already analysed.

Massumi (1967) has claimed that several cases of cardiomyopathy reported in the literature have the electrocardiographic appearances of the Wolff-Parkinson-White syndrome. However, in these other cases that he cites, the features did not precisely resemble those of the Wolff-Parkinson-White syndrome or were rather atypical and more in keeping with the descriptions by Harmjanz et al. (1971). This is so in the cases of cardiomyopathy described by Campbell and Turner-Warwick (1956), Cohen et al. (1964), Soulié et al. (1957) and Westlake et al. (1962); no conclusions can be drawn from the paper by Shabetai and McQuire (1963) as they published no tracings of their cases. These latter workers claimed that the Wolff-Parkinson-White syndrome occurred in several relatives of a patient with hypertrophic obstructive cardiomyopathy; but again, no electrocardiograms were published. Their claims appear tenuous; they reported that the father of the patient with hypertrophic obstructive cardiomyopathy had paroxysmal atrial fibrillation, possible left ventricular hypertrophy on chest X-ray, and a loud apical systolic murmur. The electrocardiogram was said to show the

Wolff-Parkinson-White syndrome with premature atrial beats and aberrant ventricular conduction. The patient's sister, aged 25, had an apparently significant left parasternal systolic murmur, a normal chest X-ray, and "accelerated atrioventricular conduction" on electrocardiography. These features could be due to hypertrophic obstructive cardiomyopathy alone and it would be necessary to see the electrocardiograms in order to assess how characteristic they might be. On the limited evidence mentioned, they might just as well mimic as actually be examples of the Wolff-Parkinson-White syndrome.

Analysis of electrocardiographic tracings in another report on hypertrophic obstructive cardiomyopathy also showed features resembling rather than representing true pre-excitation. Of 33 cases of this disorder the electrocardiogram was reported as showing "anomalous atrioventricular excitation" in three (Coyne, 1968). Two of the tracings were published: both also showed left ventricular hypertrophy; in one the R waves were slurred, and in the other a delta wave was present in lead aVL. These appearances resemble those reported by Harmjanz et al. (1971), and the implication of pre-excitation is not repeated in further papers that discuss these cases (Goodwin and Oakley, 1969; Swan et al., 1971): see below.

Another case of apparent pre-excitation in cardiomyopathy is the propositus of a family in whom this disorder can be deduced (case 22 of Flensted-Jensen, 1970). This man died at the age of 29, presumably as a consequence of atrioventricular block. Only the standard limb leads were available, and over a period of 7 months, four tracings showed (a) 2:1 atrioventricular block with narrow QRS complexes; (b) sinus rhythm with QRS complexes 0.15 seconds wide and possible delta waves; (c) 3:1 atrioventricular block with narrow QRS complexes; and (d) 2:1 atrioventricular block with wide QRS complexes. It is of interest that under circumstances (a) and (c), i.e. when there was no QRS widening, the mean frontal plane axis was markedly leftwards (the tracings do not permit the actual axis to be calculated) and had the features of left anterior hemiblock (Rosenbaum et al., 1970): with the wide QRS complexes with possible delta waves, the axis had swung round to the right and the left anterior hemiblock was no longer present. In this case, intermittent left anterior hemiblock interfered with the expression of the localized pre-excitation produced by the cardiomyopathy. Evidence for the latter diagnosis includes the considerable biventricular hypertrophy at autopsy (histological specimens were unfortunately not taken), and the death of his father and sister from clinically similar illnesses.

More recently Kariv et al. (1971) have reviewed 11 families with this disorder, and have also stressed an apparent association with the Wolff-Parkinson-White syndrome. It is clear that some of these cases have previously been described (Kariv et al., 1964; 1966), but not easy to see precisely which have definitely appeared in the earlier reports. Several however, do not appear to have been described previously. Patient BUII/5 (aged 19) gave a history of palpitations for three years and had radiological evidence of cardiac enlargement; the electrocardiogram "occasionally revealed Wolff-Parkinson-White conduction", but more usually there was left bundle branch block, complete or incomplete. No tracings are published and it is thus impossible to see if the "Wolff-Parkinson-White syndrome" meets the criteria for that condition and, if so, whether of type A or type B; nor is it possible to assess the effect of the left bundle branch block on the pre-excitation pattern (see Chapters 4 and 5). Case SUII/3 (aged 43) was asymptomatic but the electrocardiogram (neither shown nor described) was said to indicate the Wolff-Parkinson-White syndrome; one year later she developed complete heart block and has required a permanent artificial cardiac pacemaker. Many members of this family clearly have cardiomyopathy. Her case resembles those described by Lev et al. (1966), Massumi (1970) and Timmis et al. (1971) as regards the development of complete heart block complicating the Wolff-Parkinson-White syndrome, but in these latter cases there was no evidence of cardiomyopathy. Case LEII/5 had already been published as case 2 (Kariv et al., 1966). Of 47 cases, 20 had disorders of cardiac rhythm, including six with complete heart block, eleven with paroxysmal tachycardia and six with atrial fibrillation: some went from paroxysmal tachycardia or atrial fibrillation to complete heart block.

Kariv et al. (1964) reported a patient who died suddenly at the age of 31. He was the son of a patient with cardiomyopathy, and he had a systolic murmur clinically. His electrocardiogram was compatible with the Wolff-Parkinson-White syndrome type B, albeit with a P-R interval of 0.16 seconds. This suggests that any communication that might have produced anomalous conduction would have arisen below the atrioventricular node, e.g. Mahaim tracts, and that there was no bypass of the atrioventricular node that would have produced shortening of the P-R interval. This patient died suddenly when he was 31 years old and at autopsy was found to have myocardial hypertrophy, with a large scar 3 cm. in diameter in the interventricular septum; the coronary arteries were normal. Unfortunately, there is no mention of appropriate studies to seek anomalous pathways. The other case in this particular paper that showed features compatible with the Wolff-Parkinson-White syndrome was case 11, who presented with palpitations when aged 7. This patient has a mitral systolic murmur and radiological evidence of left atrial enlargement. The arrhythmia had been documented as atrial fibrillation. During sinus rhythm the normal complexes (showing moderate left ventricular hypertrophy) alternated with the features of the Wolff-Parkinson-White syndrome, type A.

In some of these cases there was clearly at times Wolff-Parkinson-White conduction; however, most would appear to have been patients with cardiomyopathy whose disorder produced an electrocardiogram that mimicked pre-excitation. It is possible that one of their cases of the Wolff-Parkinson-White syndrome is also described elsewhere by one of the authors: Sherf and James (1969) illustrate a case of familial cardiomyopathy in whom one electrocardiogram showed a P-R interval of 0.20 seconds and a QRS of 0.08 seconds, without slurred R waves, but with signs of left ventricular hypertrophy. A subsequent tracing showed different P wave morphology, a P-R interval of 0.15 seconds, QRS 0.10 seconds, marked leftward shift of the QRS axis, and slurred R waves well seen in the precordial leads: features quite compatible with the Wolff-Parkinson-White syndrome type A.

Turning now to some other reports, one encounters further cases in whom cardiomyopathy may be linked with the Wolff-Parkinson-White syndrome, or in whom there might just be a resemblance. Of 48 cases of the Wolff-

Parkinson-White syndrome seen in 10,000 children, the heart was normal in 28 cases (Swiderski et al. 1962). In 20 there were a variety of lesions, but the most common congenital abnormalities were the Ebstein anomaly (4) and corrected transposition of the great vessels (3). They reported five cases as having suffered from "primary myocardial disease." Two of these were siblings with cardiomyopathy. One of these cases died and the diagnosis of cardiomyopathy was confirmed at autopsy; the presence of a bypass is not mentioned in the paper and one cannot necessarily conclude that it was absent, as there was no indication that special sectioning had been carried out. The electrocardiograms of this case were published, and show a P-R interval of 0.12 seconds with QRS complexes 0.12 seconds wide. Slurring of the upstroke of the R wave is evident in this case, in tracings taken during sinus rhythm, during paroxysmal atrial tachycardia with 2:1 block, and atrial fibrillation. These features closely resemble those of Case 21 and probably provide a further example of apparent preexcitation rather than the real thing. Neither the tracings nor a description of the electrocardiogram of the surviving sibling appear in this article and no conclusions can be drawn.

The electrocardiograms of the remaining three cases with primary myocardial disease were not published either. One case was described as having had the Wolff-Parkinson-White syndrome type B demonstrated during an attack of myocarditis suffered at the age of 7 weeks, with consistently normal tracings since then until the report appeared when the patient was five years old. There had been no attacks of paroxysmal tachycardia. It is possible that the myocarditis in this case acted as a stimulus to the expression of pre-excitation in the way considered in Chapter 12. The fourth case was a boy seen at the age of six with the Wolff-Parkinson-White syndrome type B and paroxysmal atrial tachycardia; he died at the age of ten due to congestive cardiac failure and there was no autopsy. The fifth case was first seen when 7 months old because of paroxysmal atrial tachycardia, and the Wolff-Parkinson-White syndrome type B was then recognized and consistently seen on subsequent electrocardiograms until death at the age of 20, apparently due to an arrhythmia. Autopsy revealed old aortic and mitral valvulitis and hypertrophy and fibrosis of the myocardium; no mention was made of a search for a bypass.

Despite the fact that there have been these isolated cases reporting the Wolff-Parkinson-White syndrome as being characteristic of, or occurring in, cardiomyopathy, attention must be paid to two large and well-documented series. Only one of 23 cases of hypertrophic obstructive cardiomyopathy studied by Meerschwam (1968) had delta waves, and these were small; none had the classical features of the Wolff-Parkinson-White syndrome, but eleven had abnormally deep and broad Q waves, simulating myocardial infarction. Also of great importance is the work of the Hammersmith group (Swan et al., 1971). These workers followed 85 patients for ten years or more and none had the classical Wolff-Parkinson-White syndrome. Six of these had short P-R intervals (less than 0.13 seconds); two appear to have had delta waves though without QRS prolongation. In their general experience, they thought that the P-R intervals were usually within the lower ranges of normal in their patients, but they did not specify figures. They only encountered atrial fibrillation in four of these cases: in three it was paroxysmal and in one established. They thought that atrial fibrillation, when it occurred, was usually a feature of advanced hypertrophic obstructive cardiomyopathy. The delta waves in the two cases might well have been examples of the type seen in Cases 21-24; the precise significance of the apparent shortening of the P-R intervals is difficult to assess; but cases like this merit intracardiac studies with His bundle electrography in order to establish where, if at all, any apparent shortening of conduction time occurs between the sinoatrial node above and the commencement of the process of intraventricular conduction below.

Presumably this series may have included a case published by Goodwin and Oakley (1969) in which features similar to those presented herein are seen in patients with both hypertrophic and congestive cardiomyopathy. The most impressive case is their figure 60, an electrocardiogram from a 10-year-old boy, who had left ventricular hypertrophy, a normal P-R interval (0.18 seconds) and slurring of the upstroke of R in leads I, II and V4-7. They suggest that this resembled type

B pre-excitation (Wolff-Parkinson-White), but clearly recognized that this was not the true bill. Another electrocardiogram, their figure 6b, shows a pattern resembling anteroseptal cardiac infarction, but also with slurred R waves in leads I, V3 and V4. Of particular interest, because Cases 21, 22, 23 and 24 appear to suffer from congestive cardiomyopathy, is the very similar appearance seen in one of their cases, in their figure 3a.

As Oakley (1971) has pointed out, congestive cardiomyopathy is a form of systolic pump failure, primary in origin in that other possible causes like hypertensive heart disease with failure, constrictive pericarditis and ischaemic heart disease have been excluded. This is to be distinguished from diastolic compliance failure secondary to myocardial hypertrophy, i.e. hypertrophic cardiomyopathy, which may exist without obstruction to left ventricular ejection. In this disorder the hypertrophy is now thought to be a property of the abnormal myocardial cell not secondary to haemodynamic stress resulting from outflow tract obstruction. Olsen (1971) has been able to demonstrate pathological differentiation between these two disorders on the basis of light microscopy, ultrastructure, and histochemical changes. However, no electrocardiographic study has attempted to differentiate between these two disorders; it is possible that any electrocardiographic resemblances between hypertrophic and congestive cardiomyopathy might reflect changes occurring in specific areas rather than qualitative ones reflecting the differences in the pathological processes producing them. Even though Van Dam et al. (1972) have studied cases of hypertrophic obstructive cardiomyopathy with left ventricular outflow obstruction, it may well be that the electrophysiological changes that they saw were due to the disease process other than the obstruction.

That these electrocardiographic changes are not specific to hypertrophic cardiomyopathy is evident from the sample tracing (their figure 3) and comments of McDonald et al. (1972) in "non-obstructive primary cardiomyopathy". Their cases conform entirely with Cases 21-24. They found "slurred, notched and deformed R waves of diffuse myocardial disease and defective intraventricular conduction" in three-quarters of their patients. Their typical electrocardiogram has slurred R waves, resembling delta waves, in leads I and aVL (in the other leads it is less easy to see the appearances, for technical reasons). Of their 31 cases, four had atrial fibrillation and one had paroxysmal atrial tachycardia.

As Goodwin (1970) has pointed out, it may be difficult to distinguish between "hypertrophic" and "congestive" cardiomyopathy, especially in terminal cases. Case 21 resembles other patients who would best fit into the category of asymptomatic "congestive" cardiomyopathy - asymptomatic save for the attacks of paroxysmal arrhythmias, yet with clinical radiological and electrocardiographic features of cardiac hypertrophy. There is no family history of similar disease, but many relativeslive abroad and the presence or absence of such disorder cannot reliably be established. The finding of a delta wave is one pointer to the diagnosis of obstructive cardiomyopathy if the statistical criteria of Braunwald et al. (1964) or the explanations of Harmjanz et al. (1971) are to be considered. Cases 21, 22, 23 and 24 appear to be sporadic cases of cardiomyopathy but, as Emanuel et al. (1971) have shown, there appear to be dominant and recessive modes of inheritance in both "hypertrophic" and "congestive" cardiomyopathies, and full information on family histories is lacking.

This, then, is the current picture. Somewhat similar electrocardiographic features and the occurrence of arrhythmias may cause confusion between cardiomyopathies and the Wolff-Parkinson-White syndrome. Only rarely do they co-exist, and then the problem is to decide whether there is a causal or chance association in the individual case. On theoretical grounds, the former may occur. The possible ways in which this can happen - albeit, it would seem, rarely - may throw light on presently ill-understood aspects of why anomalous bypasses may or may not conduct impulses.

The present perspective of the possible relationship between cardiomyopathies and the Wolff-Parkinson-White syndrome is thus a blurred one; and even less is known with regard to the Lown-Ganong-Levine syndrome. Sherf and James (1969) have suggested mechanisms whereby cardiomyopathy could produce these syndromes, but this concept remains hypothetical. What is clear is that cardiomyopathies can, on the electrocardiogram, show features simulating pre-excitation. Wherever true pre-excitation appears to be present, intracardiac electrography provides the only clinical means of confirmation. Thorough pathological examination of hearts from those who die with these disorders provides the basis for fundamental understanding in the future.

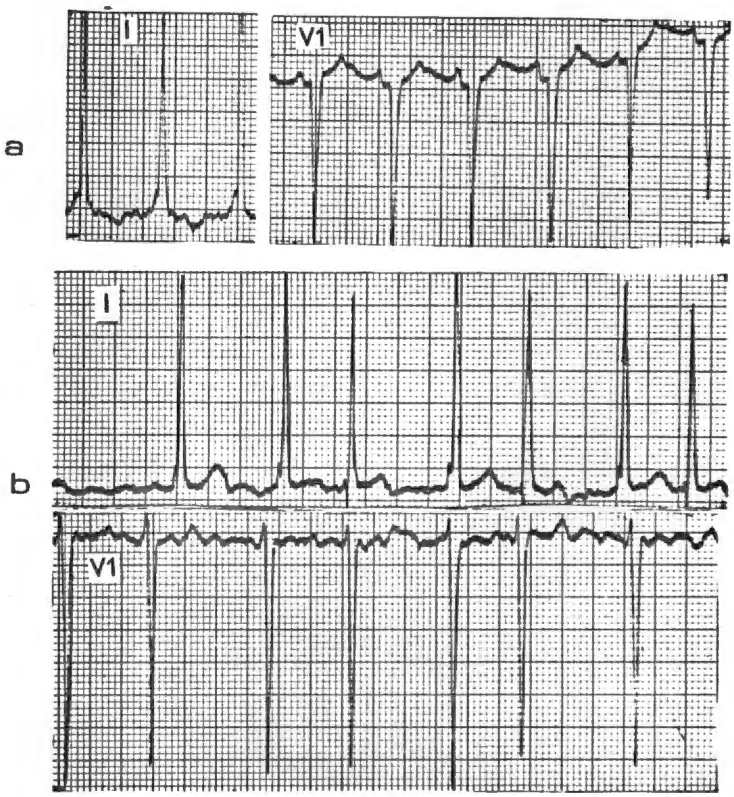


Figure 73 (Case 21) Electrocardiographic strips (leads I and V_1), showing

(a) paroxysmal tachycardia or atrial flutter, with 2:1 block.

(b) atrial fibrillation.

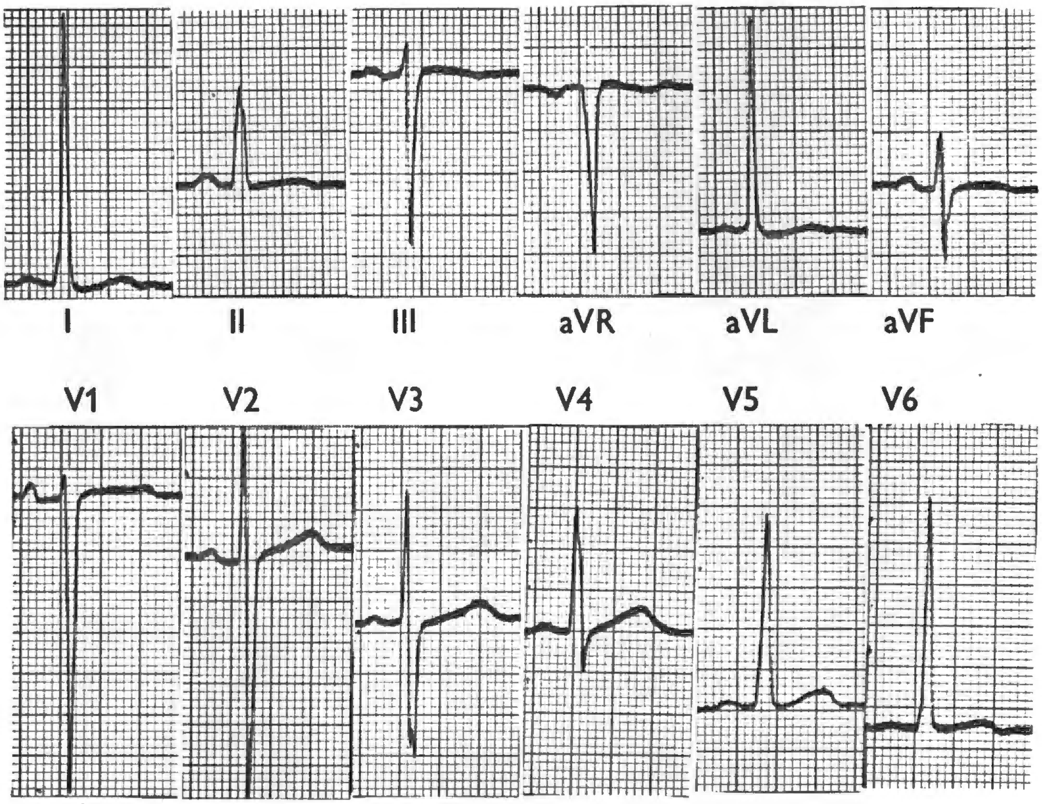


Figure 74 (Case 21) Electrocardiogram, sinus rhythm.

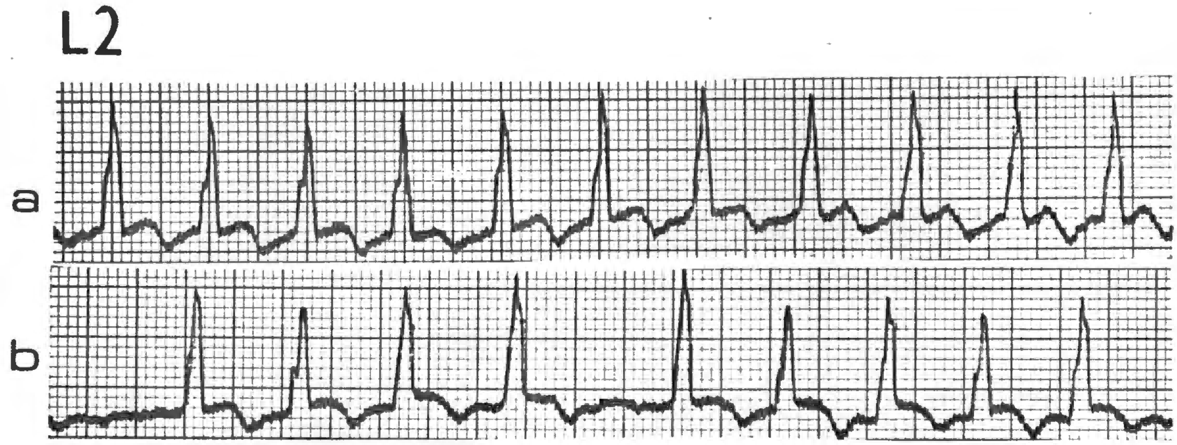


Figure 75 (Case 21) Electrocardiographic strip showing
(a) paroxysmal tachycardia; and
(b) atrial fibrillation.

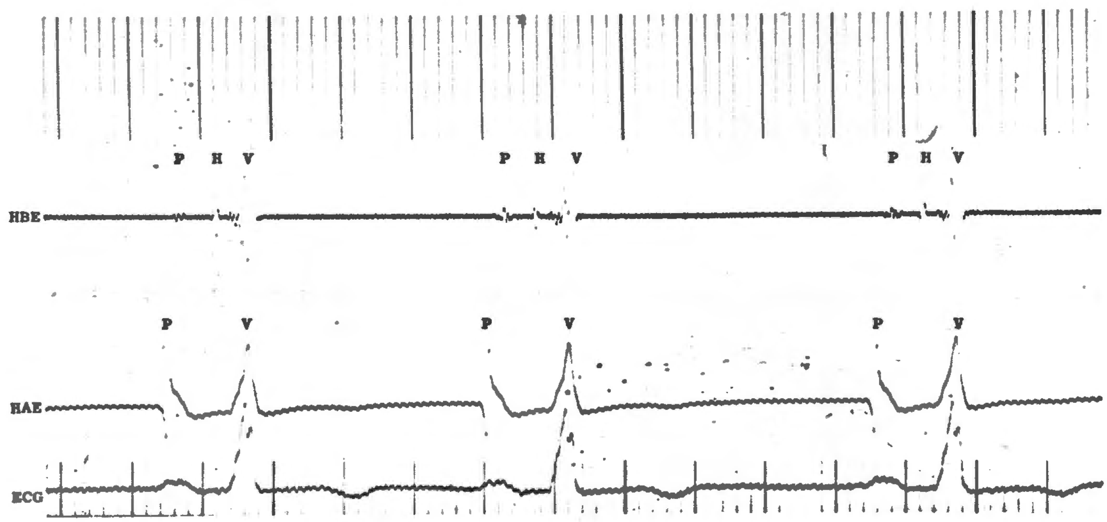


Figure 76 (Case 21) His bundle electrogram (HBE), high right atrial electrogram (HAE) and electrocardiogram (ECG). In the HBE lead, P = atrial activation; in HAE, P = P wave proper. Sinus rhythm.

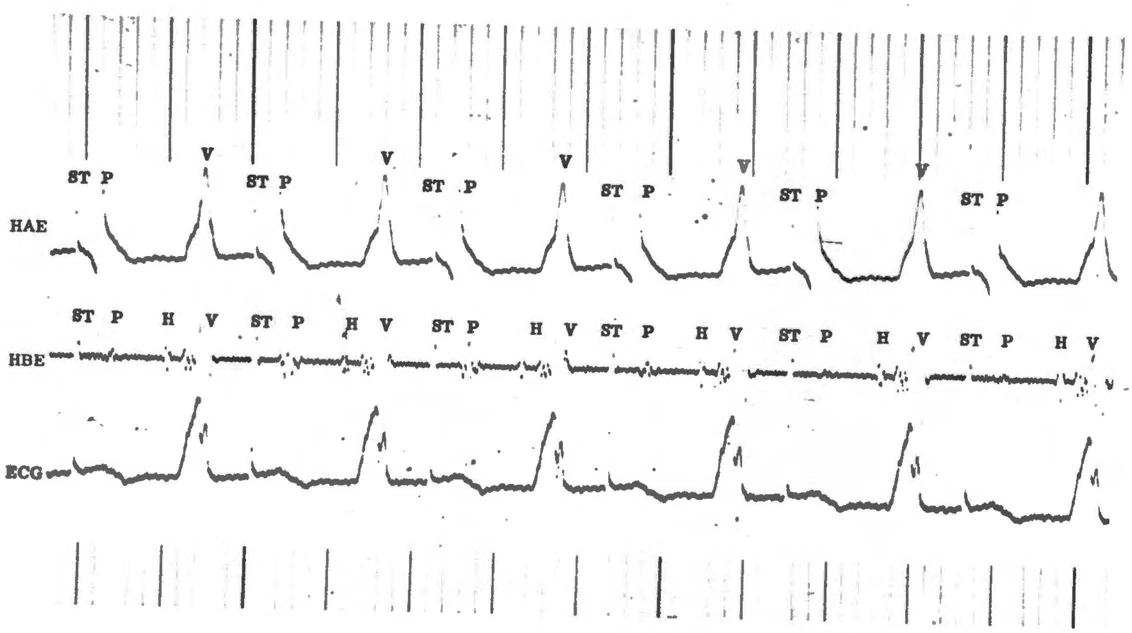


Figure 77 (Case 21) His bundle electrogram, high right atrial electrogram and electrocardiogram, during right atrial pacing (148 beats a minute). ST = stimulus artefact.

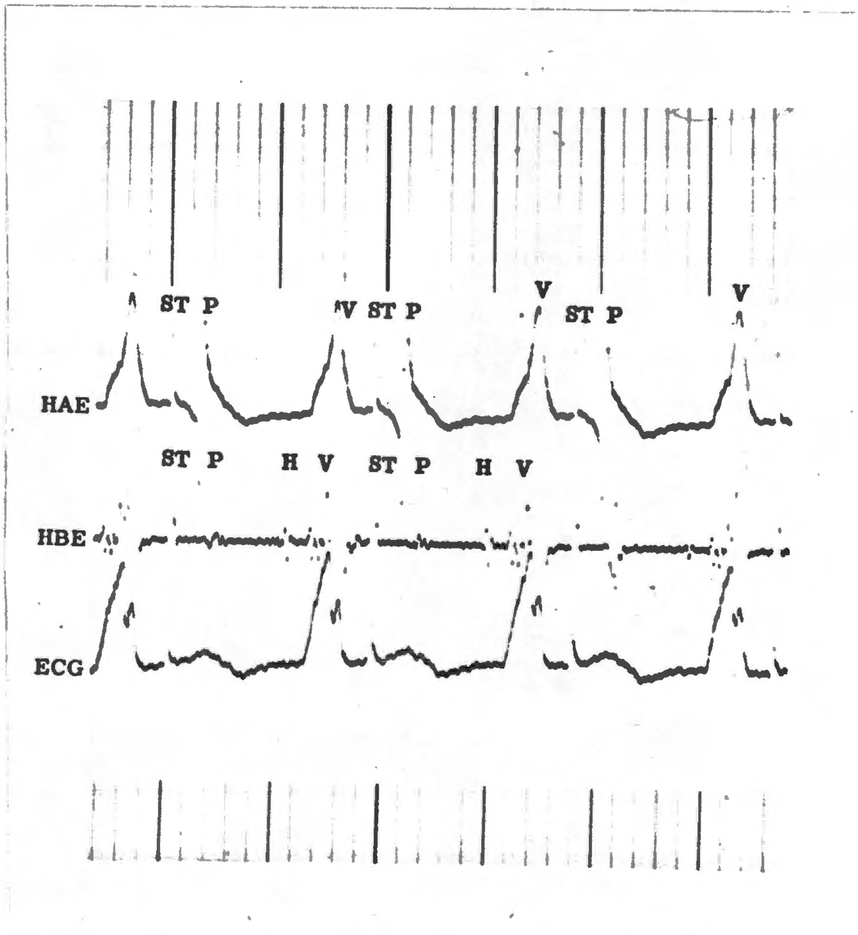


Figure 78 (Case 21) His bundle electrogram, high right atrial electrogram and electrocardiogram, during right atrial pacing (158 beats a minute).

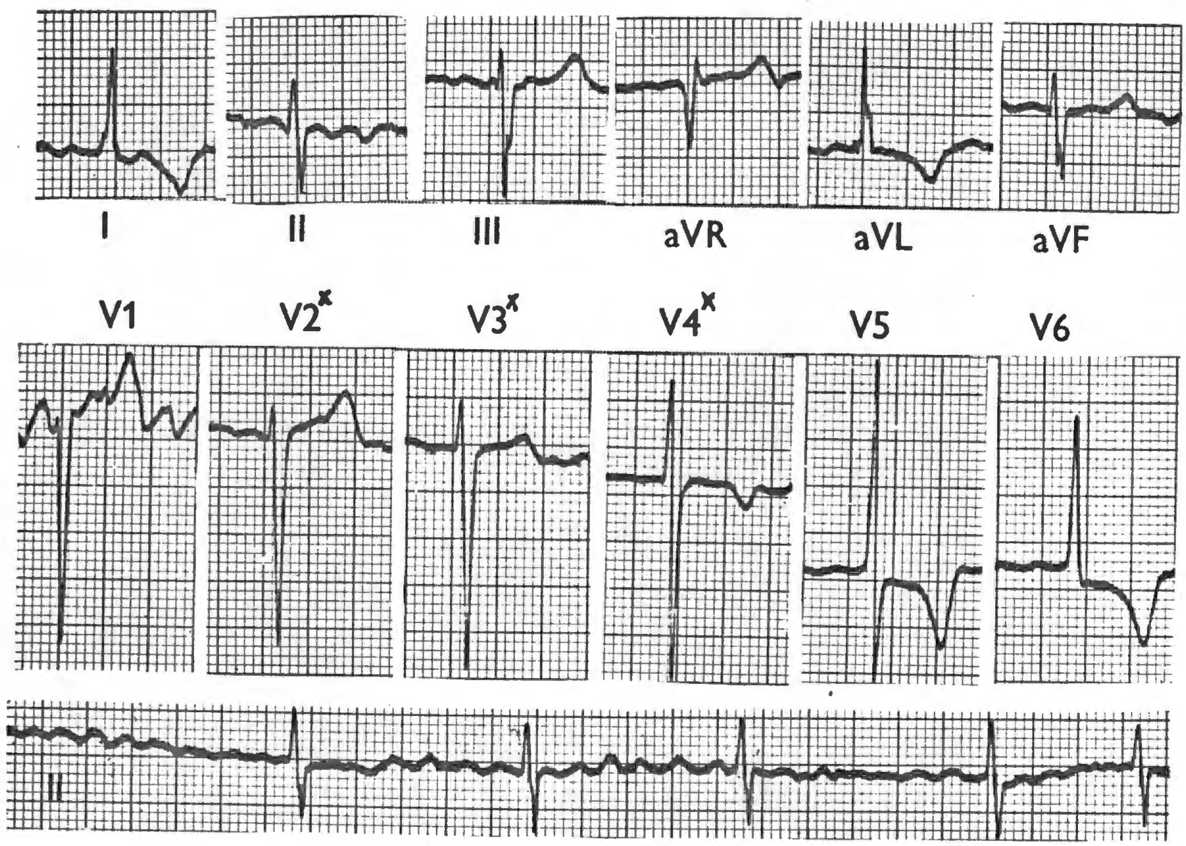


Figure 79 (Case 22) Electrocardiogram: leads V2, V3 and V4 recorded at half voltage.

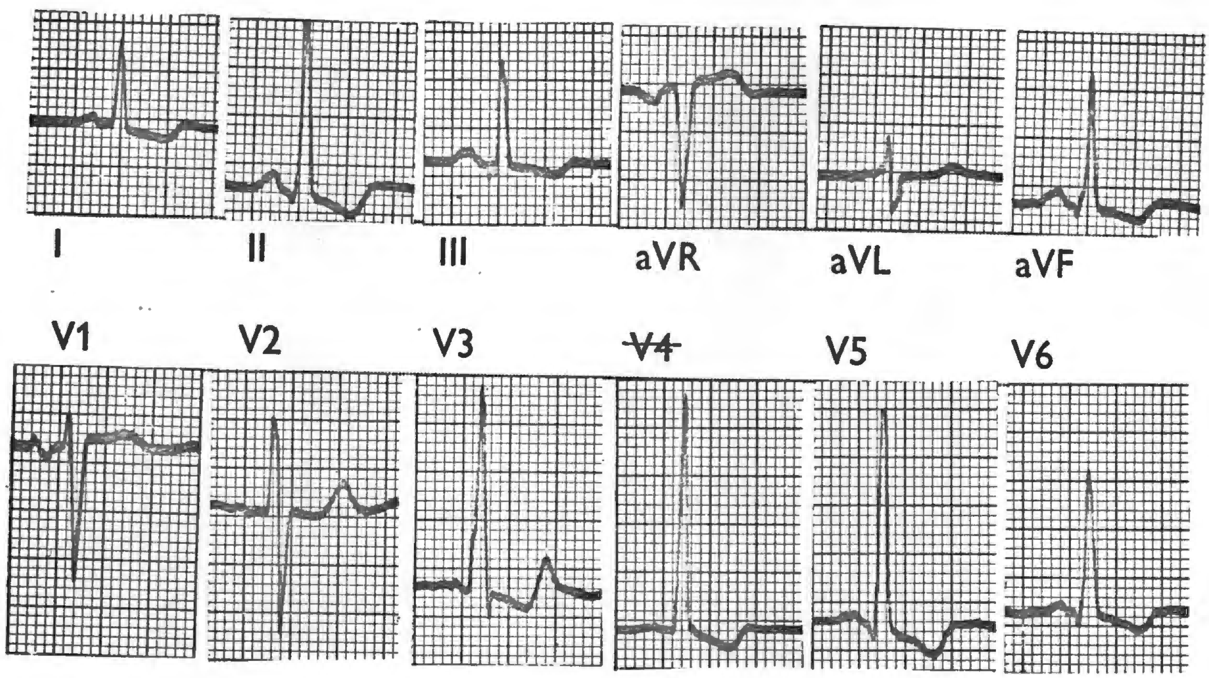


Figure 80 (Case 23) Electrocardiogram: V4 recorded at half voltage.

Figure 84 (Case 23) Electrocardiographic strips (continuous) showing regularization of atrial fibrillation after intravenous verapamil.

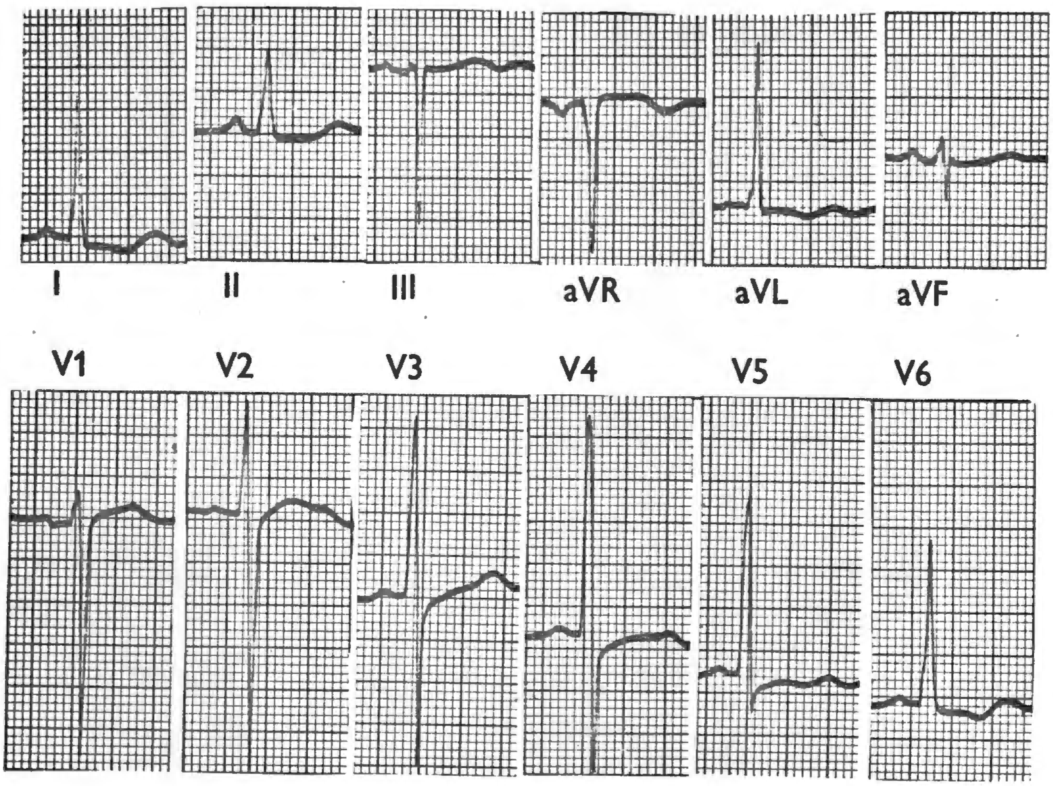


Figure 82 (Case 24) Electrocardiogram, with apparent delta waves most easily seen in aVL and V6, and moderate left ventricular hypertrophy.

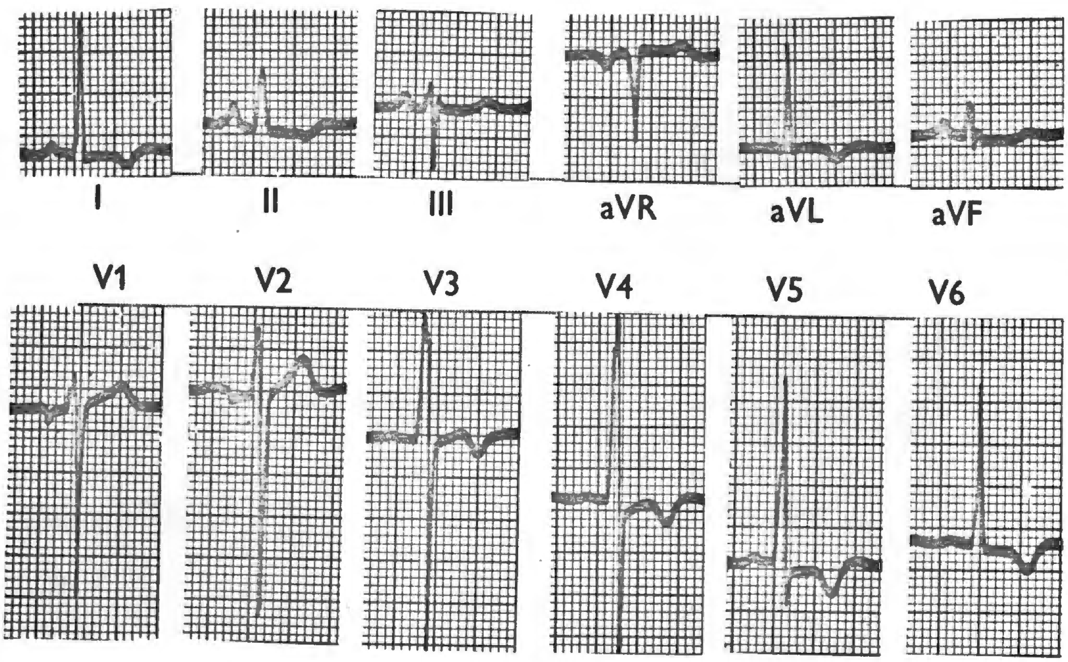


Figure 83 (Case 24) Electrocardiogram, with gradual slurring of upstroke of R noted especially in V4-6, and gross left ventricular hypertrophy.

CHAPTER 14

"Miscellaneous Mimics"

It is not just cardiomyopathy that may erroneously suggest the Wolff-Parkinson-White syndrome. Under certain circumstances other disorders may resemble it, and three particular examples have been chosen to illustrate these possibilities.

Incomplete left bundle branch block

That incomplete left bundle branch block may be one mechanism of causing appearances like those of the Wolff-Parkinson-White syndrome has already been discussed in Chapter 13. Its occurrence in ischaemic or hypertensive heart disease, or due to another cause of conduction disturbance, was for long doubted, but the existence of this entity was validated by Schamroth and Bradlow (1964). Allusion has been made in the previous Chapter to Case 25, who illustrates this situation. He was on maintenance digoxin throughout.

The first electrocardiogram (Figure 84) is representative of seven tracings recorded between 1968 and 1971, and shows sinus rhythm at the rate of 80 beats a minute, a P-R interval of 0.14 seconds, and QRS 0.08 seconds. There are tall R waves in V5 and deep S waves in V2 (total 90 mm.), with ST depression in leads I, II, aVL, V5 and V6, and T wave inversion in leads II, III, aVF, V5 and V6; T-I is biphasic. These changes conform with the presence of severe left ventricular hypertrophy. In addition there are deep Q waves (0.04 seconds wide) in III and aVF, narrow Q waves in V5 and V6, and also a minute Q-II. The precordial Q waves are consistent with left ventricular hypertrophy; the inferior changes could mean old cardiac infarction. The poor increase in the size of the R wave across the precordium from V1 to V4 is consistent with septal hypertrophy; one does not need to invoke healed anteroseptal cardiac infarction. Quite apart from this, there is slurring of the origin of the R wave in leads II and aVL, and of the Q wave in leads III and aVF.

Although there was no acute episode, the electrocardiographic appearances changed during 1971, and Figure 85 shows the recent features. Rate and rhythm, ST segment depression, and Q wave changes in leads III and aVF persist, though the T waves are no longer inverted in V5 and V6. Both the P-R interval (0.16 seconds) and the QRS complex (0.10 seconds) are slightly wider. The most significant changes are the loss of

The Q waves in leads II, V5 and V6 and of the R waves in V1 and V2 (they are also now minute in V3 and V4); with this, the slurring of the origin of R is more obvious in leads II and aVF and has also become apparent in V5 and V6, being now indistinguishable from typical delta waves.

Could Figure 85 indicate the Wolff-Parkinson-White syndrome, type B? If this were so, the longer P-R interval would indicate an exclusively infranodal bypass of the Mahaim type. By V3 one should have had tall R waves with positive delta waves and associated ST-T changes; and shift in the QRS axis should have been produced as a result of the anomalous ventricular excitation. The features are considered to represent the modification of the pre-existing signs of left ventricular hypertrophy because of the supervention of incomplete left bundle branch block, leaving unaltered the appearances possibly due to old inferior cardiac infarction.

<u>End-diastolic ventricular extrasystoles</u>

End-diastolic ventricular extrasystoles may well cause appearances that resemble the Wolff-Parkinson-White syndrome; and a series of these could easily cause the uninitiated to infer alternating normal and anomalous conduction. This is because the P waves occur at the correct time, but are followed almost immediately by the QRS of the ventricular extrasystoles; and the form of these is altered so that the combined fusion complexes resemble the Wolff-Parkinson-White syndrome, by virtue of their location in the cardiac cycle. This is exemplified in the tracings shown in Figure 86, recorded from Case 26. The basic cardiac rate of the sinus beats is 108 a minute, with an R-R interval of 0.52 seconds. The P-R interval is 0.16 seconds. In the upper panel of this non-continuous electrocardiographic tracing, the third complex is a late, end-diastolic, ventricular extrasystole. The P-R intervals between the first two complexes and the second two complexes are identical, 0.14 seconds, and the P-R interval is extremely short, being 0.07 seconds. It is followed by a QRS complex that is different in configuration from those noted during normal conduction, with a slurred upstroke that resembles a delta wave, and ST depression and T wave inversion. The R-R interval between the second and third beats is 0.44 seconds instead of

0.54, and the R-R interval from this different-looking beat to the ensuing normal-looking QRS complex is 0.62 seconds. This clearly indicates that this is a ventricular extrasystole, and as it occurs late in diastole, indeed towards the end of diastole, it follows the normal P wave, and fusion of the conduction from the sinoatrial node down the normal pathways with the depolarization induced by this extrasystole yields appearances closely resembling those seen in the Wolff-Parkinson-White syndrome.

In this patient, extrasystoles were seen at varying times during the cardiac cycle. They were however insufficiently frequent to enable a parasystolic cadence to be defined. An example of an earlier extrasystole was seen in the lower panel, recorded some minutes later, in the same lead, and from this it can be seen that the ventricular extrasystole has the more characteristic appearances expected, and occurs earlier in the cycle, with an R-R interval between the preceding sinus beat and it of 0.32 seconds. Several other complexes were seen that vary between these two extremes, between the pure and characteristic form of the ventricular extrasystole is shown in the lower panel, with that seen in the upper panel where the Wolff-Parkinson-White type of complex was simulated.

That such a series of end-diastolic ventricular extrasystoles can occur in bigeminal rhythm and simulate alternating normal and anomalous conduction (as seen, for instance, in Figure 6, Case 1) was demonstrated in a patient whose records were shown during a paper by the present author at the Southern African Cardiac Society Congress in 1962.

Myocardial infarction

It is of course much more usual for the Wolff-Parkinson-White syndrome to suggest cardiac infarction than the reverse; and the possibility that cardiac infarction (like myocarditis and cardiomyopathy) can alter mismatch impedance and bring to light latent anomalous pathways has been considered. Lesser degrees of associated conduction disturbance, akin to but not due to incomplete left bundle branch block, may cause the appearances encountered in Case 27.

The electrocardiogram (Figure 87) shows sinus rhythm, (64 beats a minute), with a P-R interval of

0.18 seconds and a QRS complex 0.12 seconds wide. Small Q waves are evident in leads I, aVF and V5 and V6, and in addition there are deep broad QS waves from V1 to V4. The T waves are inverted in leads I, II, III, aVF, V5 and V6, and the ST segments elevated in leads V1-V4. In addition, examination of the tracings reveals slurring of the upstroke of R in leads II and aVF, and slurring of the Q waves in V2-V4. These changes are brought out when the tracings are taken at a faster paper speed, and Figure 88 shows the apparent delta waves much better and that they are clearly preceded by small Q waves.

This electrocardiogram shows the consequences of a severe anterior cardiac infarction, with changes as often seen with cardiac aneurysm. Left bundle branch block has previously been diagnosed in this man, but the persistence of small Q waves in left precordial leads, and the QRS axis (which is + 85^{o}), are against this suggestion. It is much more likely that the apparent delta wave is due to a localized area of pre-excitation of irregularly hypertrophic myocardium as suggested by Harmjanz et al. (1971), or to a localized conduction defect. The same arguments against true pre-excitation apply as in Case 25.

These are an indication of the other possible disorders that can - even if only vaguely - simulate some features of pre-excitation, especially the delta wave. They will rarely cause real problems in differential diagnosis, but are shown for what they are, and to indicate that an apparent delta wave must not be confused with the real thing. Application of the criteria for the diagnosis of the Wolff-Parkinson-White syndrome (see Chapter 2) will usually provide an easy means of disposing of these mimics. Further study of the pattern of cardiac excitation in such cases may help our understanding, not only of the problems they present, but of more general considerations, but this will rarely be justified by the patient's needs.

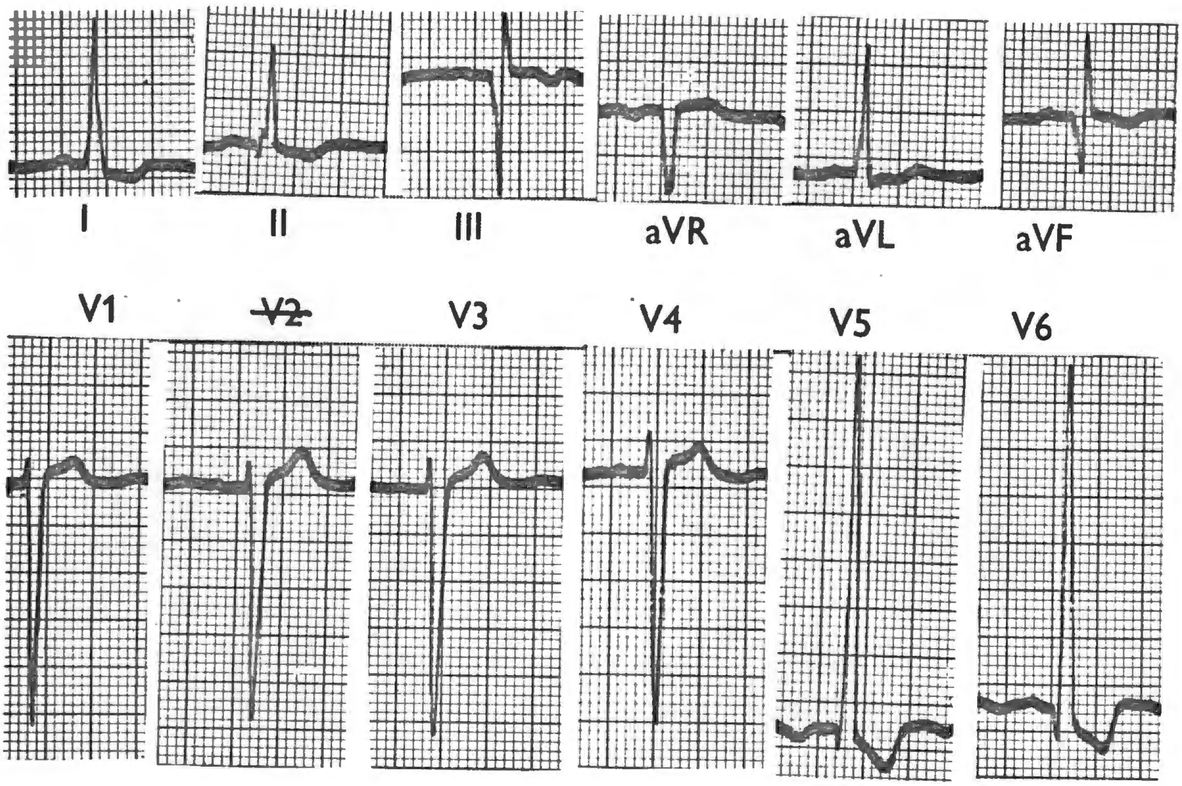


Figure 84 (Case 25) Electrocardiogram, 1970 (V2 recorded at half-voltage).

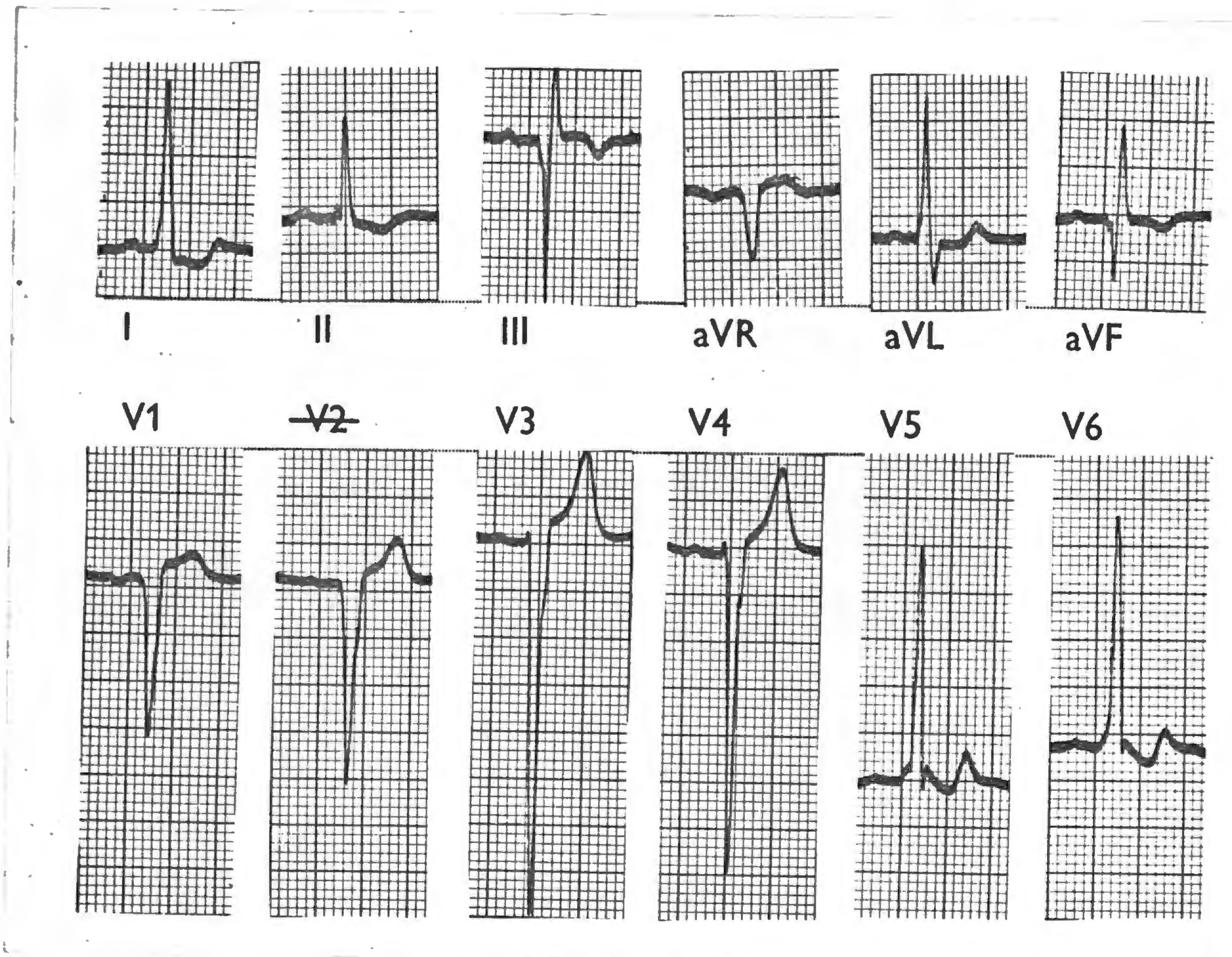


Figure 85 (Case 25) Electrocardiogram, 1972

(V2 recorded at half-voltage).

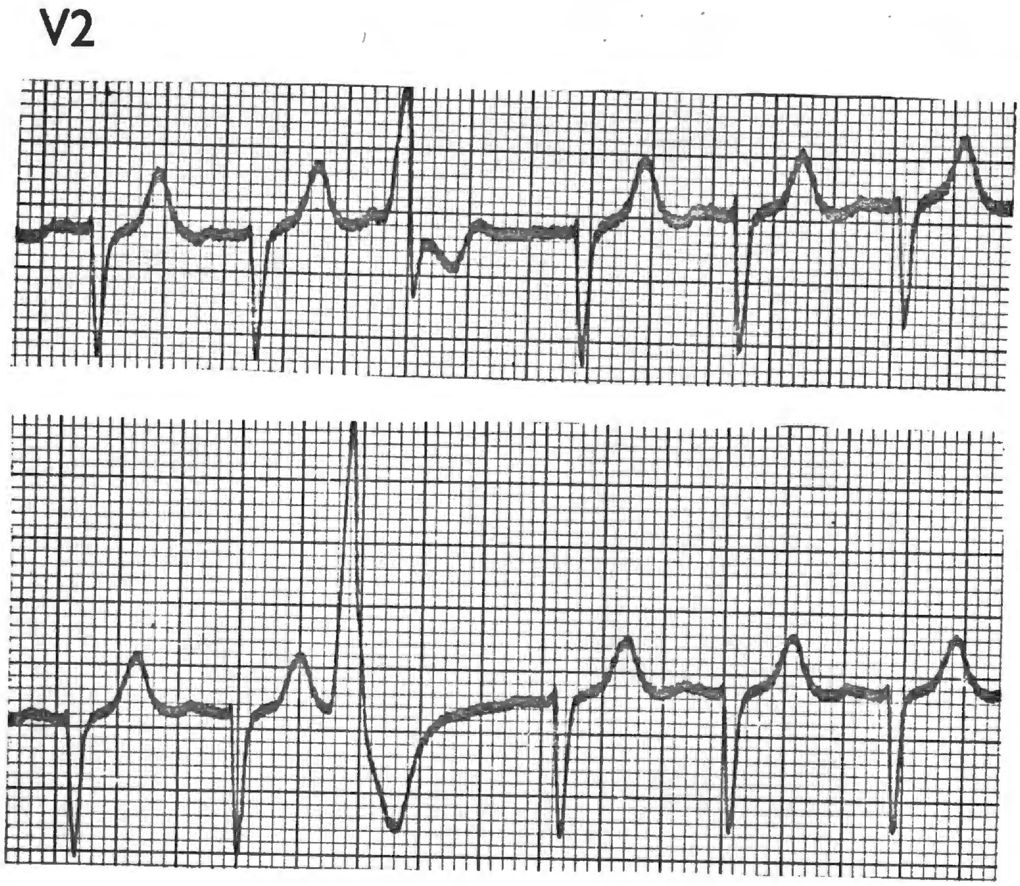


Figure 86 (Case 26) Non-continuous electrocardiographic strip (V2) showing ventricular extrasystoles, end-diastolic in the upper panel, earlier in the cycle in the lower panel.

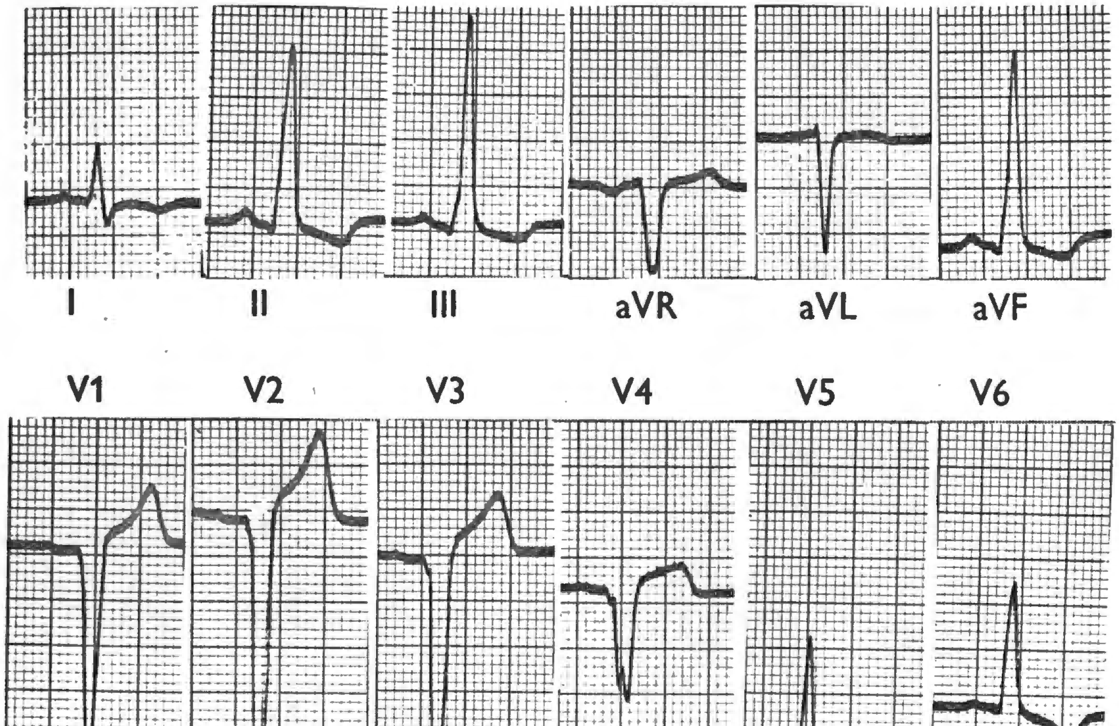


Figure 87 (Case 26) Electrocardiogram, sinus rhythm.

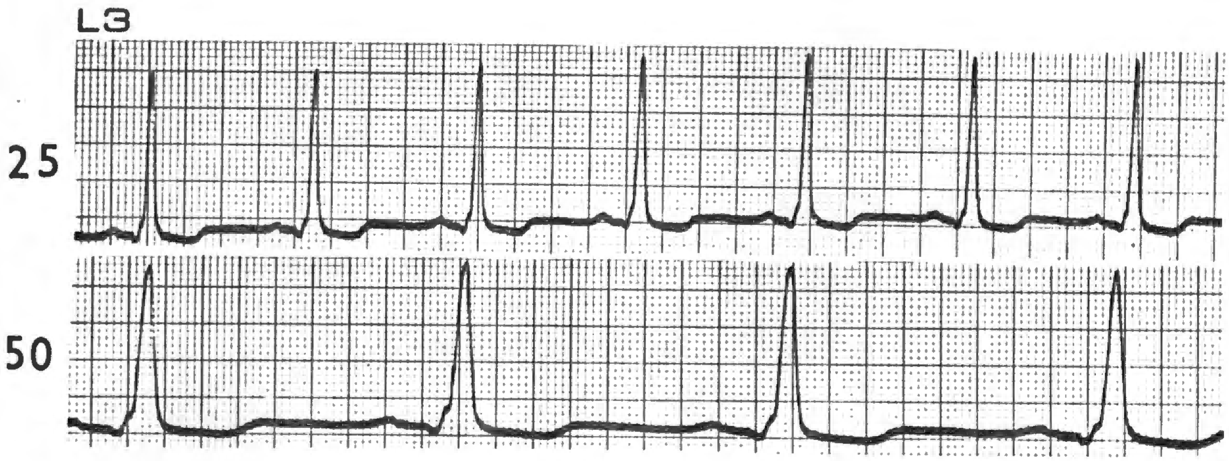


Figure 88 (Case 26) Electrocardiogram (lead III) (showing slurred upstroke of R) at normal (25 mm./second) and fast (50 mm./second) paper speeds.

SECTION C

CASE REPORTS

Clinical details and the results of pertinent investigations of the cases whose electrocardiograms are discussed in Section A and B now follow. These are presented in summary form save where specific features require more detailed exposition in order to support the arguments that are advanced.

Case 1

A 47-year-old man had for several years suffered from transient left mammary pains, stabbing in nature, usually relieved by local heat. He denied having palpitations. As a result of the electrocardiographic findings he was admitted with the tentative diagnosis of ischaemic heart disease.

There were no significant features in the past or family history. He neither smokes nor drinks. On examination he looked well and had a pulse rate of 80 beats a minute, with regular rhythm. There were no signs of cardiac failure, the neck veins were not distended and the lungs were clear and there was no oedema. His blood pressure was 120/80 mm.Hg. The heart sounds were normal and the respiratory, alimentary and nervous systems were normal likewise. Haematological and biochemical investigations were normal. X-ray of the chest showed an old calcified lesion at the right apex, which was unchanged when compared with films taken routinely in 1965: the lungs were otherwise clear. The heart was not enlarged. In the cervical spine there were minimal degenerative changes with long transverse processes to the 7th cervical vertebrae. The patient was reassured that there was no evidence of myocardial infarction, and discharged. He occasionally experiences mild left chest pains, but never any arrhythmias.

Case 2

This 40-year-old male orthopaedic surgeon is extremely fit, still playing rugby and squash without ill-effect. He presented because four days previously he had felt faint after dinner, and had been seen by a physician who recorded an electrocardiogram (Figure 11). As a result, cardiac infarction was suspected and the patient was admitted to another hospital. No physical abnormalities were found, and the clinical features did not suggest that he had suffered an infarct. He appeared quite well, with a pulse rate of 70 beats a minute, and a blood pressure of 120/80 mm. Hg. There were no cardiovascular, respiratory, alimentary or nervous abnormalities and the urine was normal. A full blood count, serum transaminases and lactic dehydrogenase, serum lipids and X-ray of the chest were all normal. The diagnosis of the Wolff-Parkinson-White syndrome was made and its variability demonstrated (Chapter 3: Figures 11, 12 and 13), and he was discharged from hospital.

At the time of this admission, the patient indicated that he was aware that there had always been something unusual about his heart. Even before he started school, in early childhood, he might develop sudden attacks of regular tachycardia of brief duration, usually resolving spontaneously in 10-15 seconds. He himself learned a trick which enabled him to stop them at will; if they lasted more than this amount of time, or if they occurred during athletics or at other times when they were inconvenient, he gave himself a sharp thump with his hand, over the middle of his sternum; and this never failed to work. He had been recognized as having an unusual electrocardiogram when he was a medical student at the London Hospital, when he was able to demonstrate that he could alter the form of his cardiac complexes by altering his heart rate using vagotonic or vagolytic measures. This was not however recognized as the Wolff-Parkinson-White syndrome and he ignored this finding as attacks had tended to become less frequent and not at all uncomfortable as the years have passed. He did not appear to have had paroxysmal tachycardia when he felt faint; the precise explanation for this was not established, but he has remained perfectly well since and has continued with his sporting activities.

It is interesting that his own self-observation of the effects of vagal stimulating and suppressing mechanisms were so closely in accord with what Wilson (1915) had first found. Parenthetically it is salutary that this diagnosis was not made when an electrocardiogram was recorded at his hospital, where Sir John Parkinson had previously been cardiologist. The other interesting point is his anticipation of the observation by Semple (1968) that a thump on the chest could stop supraventricular tachycardia, later reported in paroxysmal ventricular tachycardia by Pennington et al. (1970).

Case 3

This 70-year-old man had always enjoyed good health until six months before admission when he developed attacks of severe epigastric colic and was found to have gall stones. When he was admitted for cholecystectomy, a pre-operative electrocardiogram was recorded (Figure 24).

He denied ever experiencing palpitations, had worked hard as a cabinet-maker until he had retired five years previously, and did not have dyspnoea or any other cardiac symptoms.

Examination revealed a moderately obese man who looked very well for his age, and whose blood pressure was 140/95 mm. Hg. The heart was not enlarged clinically, and the sounds were normal. There were no abnormalities in the respiratory, alimentary or nervous systems, the urine and a chest X-ray were normal, and the remainder of the routine investigations were likewise normal. These included random blood glucose, blood urea and haemoglobin.

Case 4

A 31-year-old male printing worker had always been in excellent health and undertook strenuous physical exertion without ill-effect. He had undergone a life assurance examination and was failed with the diagnosis of "old silent inferior cardiac infarction." He was referred for further assessment, and denied any physical symptoms whatsoever or any past history of any significant illness. In particular, he had never experienced paroxysmal tachycardia.

Physical examination revealed a well-built man, 6' tall, who weighed 185 lb. There were no physical abnormalities on examination, his pulse rate was 64 beats a minute, and his blood pressure was 125/80 mm.Hg. Chest x-ray and the urine were normal.

Even superficially, the resemblance of the tracing to inferior cardiac infarction (Figure 16) could easily be dismissed once the pattern of the Wolff-Parkinson-White syndrome had been recognized; but the change from a broad QS in leads III and aVF to clearly normal appearances after atropine fully excluded this suggestion.

Case 5

The patient is a 74-year-old male who is now retired, but who had worked actively as a merchant until the age of 65. He was passed fit into the British Army at the age of 19, in 1916, and saw service in France, in the front line. After one year he experienced sudden attack of palpitations, and was examined by a military doctor who diagnosed valvular disease of the heart; and he was discharged from the Army. He was able to continue normal life, but on two or three occasions a year suffered from sudden regular palpitations which started and ended very briskly, during which he was short of breath and frightened. Their duration averaged 5-10 minutes, and a few minutes after the end of an attack, he would be able to return to his previous activity. In 1957 he suffered a longer attack, 20 minutes in duration, and when subsequently examined an electrocardiogram was recorded for the third time: this showed the Wolff-Parkinson-White pattern, Type A. Between 1957 and 1966 attacks occurred approximately 8-10 times a year and averaged 10-30 minutes in duration.

Between 1966 and 1970 he took propranolol 160 mg. daily, and this was very successful in reducing the frequency and duration of the attacks, but he had to interrupt the treatment from time to time because of dyspnoea and occasional wheezing. Since 1970 he has taken practolol 400mg. daily with equally good control and no complicating dyspnoea. Between 1960 and 1969 he was kept on digoxin, after initial digitalization, at a maintenance dose of 0.25 mg. twice daily. In 1958 he underwent prostatectomy, without ill-effect.

Examination revealed a cheerful, well-looking man, apparently youthful for his years, who was moderately obese, being 5'8" tall and weighing 170 lb. The peripheral pulses were all normally palpable, and the heart was not apparently enlarged clinically. The first and second sounds were normal and there was a Grade 2/6 aortic ejection systolic murmur. The blood pressure was 180/100 mm.Hg. The respiratory system was normal apart from slight expiratory prolongation. The alimentary and nervous systems and the urine were normal.

X-ray of the chest showed no evidence of cardiomegaly, but bronchopulmonary markings were slightly increased and the lungs were slightly over-inflated. At various times during the period of observation the following blood investigations had been done and had always been normal: full count, sedimentation rate, glucose, urea, cholesterol and electrolytes.

Case 6

The patient was a 31-year-old engineering worker who was admitted to hospital because of severe retrosternal chest pain that radiated to his left arm and leg and that was accompanied by dyspnoea. Four years previously he had first collapsed with chest pain and was investigated elsewhere and treated with anticoagulants. Since then he had had frequent episodes of chest pain, unrelated to exertion, which were sometimes apparently helped by glyceryl trinitrate. Three months prior to admission he had been admitted to another hospital with severe chest pain and initially treated with anticoagulants, which were continued as an out-patient, but then discontinued because the pain persisted and was thought not to be organic.

On no occasion has the patient complained of palpitations. On several occasions during these four years he has complained of coughing up blood, and says that on one occasion he was told that he had a scar on his lung. Three months previously when he attended a different hospital it was suspected that he might have pulmonary embolism arising from deep venous thrombosis, but bilateral venograms were normal.

There were no significant features in the family history; his father had died of rheumatic heart disease, but he said that no other close relatives had suffered from any cardiac disease. He smoked 10 cigarettes a day and said that his consumption of alcohol was moderate. The only medications that he had been taking recently were glyceryl trinitrate for his chest pain.

Examination revealed an anxious, pale, man, who was sweating profusely and who looked unwell. His pulse was regular at the rate of 92 beats per minute and the peripheral pulses were all normal. The blood pressure was 120/85 mm. Hg. The heart was not enlarged clinically, and there were no signs of cardiac failure, no added sounds, and no cardiac murmurs. Neither leg was swollen, but he complained that the left calf was tender when it was palpated. The respiratory, alimentary and nervous systems were all normal. The urine was likewise normal.

Full blood count, sedimentation rate, blood urea and electrolytes and blood glucose were normal, as were the serum transaminases (aspartate, 16 units; alanine 31) and lactic dehydrogenase (44 units).

X-ray of the chest showed ill-defined opacities at the left base, which did not change in a further three films taken over the next three weeks.

It was initially felt by those responsible for his care on admission that he had suffered from cardiac infarction. They did not recognize the electrocardiographic features as indicating the Wolff-Parkinson-White syndrome and concluded that he had suffered from anteroseptal and inferior cardiac infarction; he was given anticoagulant treatment (warfarin). He continued to complain of vague chest pains, and with the radiological appearances in the chest, the clinical diagnosis was tentatively altered to that of deep venous thrombosis with multiple pulmonary embolism. In consultation, the electrocardiographic features were then identified, and it became clear that some others had previously made this diagnosis. Anticoagulant treatment was discontinued, and a psychiatrist felt that his behaviour represented an hysterical reaction akin to the Munchausen syndrome, and recommended further in-patient psychiatric care, whereupon the patient discharged himself from hospital. Further attempts at follow-up have proved unsuccessful.

Here we are dealing with a psychiatrically-disturbed individual who has two positive findings on investigation which have led to concern among those seeing him, and the institution of therapy that on reflection does not appear to have been justified. He has had similar radiological changes in his lungs that have not altered over a four-year period as judged from the various hospital records. Given the history of haemoptysis and with calf tenderness on pressure, this combination has suggested pulmonary embolism, for which he had undergone venography and on at least two occasions has received anticoagulants. Furthermore the chest pain, radiating to the arm, has suggested cardiac infarction, and the bizarre electrocardiographic appearances have been interpreted as supporting this diagnosis, again leading to anticoagulant therapy.

Case 7

At the age of 58, this dress manufacturer developed stabbing pains in the left side of his chest, and was referred to another hospital for electrocardiography. The diagnosis of cardiac infarction was made and the patient was given glyceryl trinitrate, without relief. The pains were usually brief, unassociated with exertion, dyspnoea or palpitations, and usually occurred under circumstances of stress. Four years after the diagnosis was first made, he was referred back for review electrocardiography and the diagnosis was "confirmed." He lived a slightly restricted life on this account, and was very anxious about the possibility of death from cardiac disease.

He was admitted to hospital seven years later having suffered palpitations, severe central chest pain and faintness for more than an hour. His health in the past had otherwise been excellent, and there was no history of premature death from cardiac disease among members of the family. He smoked 20 cigarettes a day and took alcohol only on rare occasions. On admission, he was found to be a cheerful man, sweating slightly, who was not cyanosed and who showed no evidence of cardiac failure: the lung bases were clear, the neck veins were not distended, and there was no oedema. His pulse was grossly irregular, the rate averaging 150 beats per minute, and the blood pressure was 140/80 mm.Hg. The heart was not enlarged clinically, the apex being impalpable, and the 1st and 2nd heart sounds were heard without added sounds or murmurs. The respiratory, alimentary and nervous systems and the urine were normal. The electrocardiogram showed atrial fibrillation (Figure 58), but the duty Registrar made the diagnosis of paroxysmal ventricular tachycardia and gave intravenous lignocaine, a "bolus" being followed by a continuous infusion. Conversion to sinus rhythm appears to have taken place between one and two hours after treatment was started; the lignocaine was continued for a total period of 48 hours. No further arrhythmias took place during this admission. Normal values were obtained for a full blood count, sedimentation rate, blood urea, electrolytes, glucose and lipids. On the day after admission both serum transaminases (aspartate

104 units; alanine, 93) were elevated, but the lactic dehydrogenase (103) was normal. An x-ray of the chest was normal. His serum enzymes were repeated on the 6th day after admission and the serum transaminases had fallen to normal values of 24 units and 22 units respectively; lactic dehydrogenase was not measured.

The electrocardiogram in sinus rhythm (Figure 9) was initially misinterpreted by a registrar as indicating the presence of true posterior cardiac infarction and the patient was kept in bed with the diagnosis of cardiac infarction complicated by ventricular tachycardia. The transient elevation of the serum transaminases was taken as confirmatory evidence. The opportunity to review the tracings came two weeks after his admission, when it was recognized that he had the Wolff-Parkinson-White syndrome, type A, and that he had experienced a paroxysm of atrial fibrillation. He was then allowed up and discharged. Nine months later he suddenly developed palpitations, followed by severe central chest pain radiating into his back, faintness, and dyspnoea. He was admitted to hospital, where he was found to be collapsed, with a blood pressure of 95/85 mm.Hg, and a regular heart rate of 200 beats per minute. The heart was not enlarged clinically, and there were no added sounds or murmurs audible; there were, however, crepitations at both lung bases and the jugular venous pressure was raised 3 cm. above the sternal angle. There was no oedema, the liver was not enlarged, and no other abnormalities were found. A portable chest film showed pulmonary congestion and an electrocardiogram showed paroxysmal supraventricular tachycardia (Figure 57).

Treatment consisted of an intravenous infusion containing frusemide and lignocaine, but he was no better after 1½ hours; then he suddenly vomited, and this was followed by conversion to sinus rhythm at the rate of 80 beats a minute. His chest pain disappeared rapidly. On re-examination, he had within two hours lost the pulmonary congestion and the cervical venous distension, and a chest x-ray the following day showed there no longer to be any pulmonary congestion. No new features were found on routine investigation, but the serum aspartate and alanine were each raised to 104 units. The patient was allowed up after five days, when his blood pressure was 140/90 mm.Hg and there were no physical abnormalities. The electrocardiogram was unchanged, but after effort fairly frequent ventricular extrasystoles appeared (Figure 29): these suggested myocardial infarction. He was discharged on practolol 100 mg. twice daily but he later had a series of attacks of tachycardia with pressing central chest pain, each lasting 1-2 hours. On only one occasion an attack was stopped by carotid sinus pressure; on another occasion he needed cardioversion; other attacks took one or two hours to pass. Accordingly the practolol was stopped and long-acting quinidine (kinidin durules) 500 mg. was given twice daily. No further attacks occurred during the next three weeks, and the quinidine was stopped: within eight days he developed a very severe attack, and came to hospital where he was given an intravenous injection of verapamil (10 mgm. over 30 seconds): conversion to sinus rhythm occurred after 80 seconds (Figure 62). Thereafter he was given kinidin durules 750 mg. twice daily; few further attacks of paroxysmal tachycardia have occurred since then.

Careful interrogation of the patient leaves no doubt that the left mammary pains for which he originally underwent electrocardiography were due to anxiety. This anxiety was further compounded when the electrocardiographic tracings were misinterpreted as showing cardiac infarction. Both tracings are identical with Figure 9 in that they show the Wolff-Parkinson-White syndrome. However, he does in addition have evidence of severe paroxysmal arrhythmias. On the one occasion the atrial fibrillation was misdiagnosed as ventricular tachycardia and lignocaine was given; it seems plausible that reversion to sinus rhythm took place spontaneously. On the other occasion the vagotonic effects of vomiting appear more likely to have caused the sudden conversion to sinus rhythm than the lignocaine that he was receiving. His response to verapamil was prompt and satisfactory; at the time he had central chest pain, and this disappeared promptly as sinus rhythm was restored; this attack had not responded to carotid sinus pressure. His extrasystoles (Figures 29 and 38) were clearly shown to be ventricular in origin. With this in mind, and especially in view of the failure of practolol to prevent attacks, it was considered that an agent likely to suppress ectopic ventricular activity should be tried and long-acting quinidine proved successful. While it is difficult to be dogmatic in a disorder where the natural history may fluctuate according to other circumstances, this seems further evidence that, in this particular case, entry of ventricular extrasystoles into his abnormal pathways was responsible for the arrhythmia, for few have occurred while he has been taking this.

It seems possible that this patient in addition has ischaemic heart disease, but quite impossible to prove without the use of unjustifiable investigations. The ischaemic chest pain has only been noted during attacks in which his heart rate has been rapid, with associated ST segment depression seen during paroxysmal supraventricular tachycardia: this could be due to the tachycardia alone. While the electrocardiographic abnormalities of the pre-excitation syndrome preclude the interpretation of the tracings so as to diagnose the presence or absence of ischaemic cardiac damage, the appearances during pseudonormalization (Figure 10) and in the extrasystoles (Figure 29) suggest that he has indeed suffered from myocardial infarction, probably on the basis of underlying coronary artery disease complicated by the severe arrhythmias.

Case 8

Soon after birth this baby girl was noticed to be pale, and a loud systolic murmur was heard. When she was three months old, she developed gastro-enteritis followed by an attack of paroxysmal atrial tachycardia, at a rate of 300 beats per minute. Treatment included digitalis and chloramphenicol. A further bout of paroxysmal tachycardia was again treated with digitalis; when seen one month later she appeared healthy and had no signs of cardiac failure. The pulse rate was 114 beats a minute, and was regular. The heart did not appear enlarged clinically. There were no precordial bulges, and no thrills were palpable. The neck veins were not distended, there were no abnormal signs in the chest, and there was no oedema or cyanosis. A pansystolic murmur was best heard in the third left interspace and was accompanied by a triple rhythm. The digitalis was gradually reduced and stopped. An electrocardiogram showed the features seen in Figure 23. Phonocardiography showed an ejection-type systolic murmur, splitting of the second heart sound and a third heart sound followed by a short diastolic murmur. X-ray of the chest with screening suggested right ventricular and atrial enlargement, with normal pulmonary arterial pulsations and normal pulmonary flow. The aorta was inconspicuous. The heart was boot-shaped, and the cardiothoracic ratio was 80:130.

The diagnosis of Ebstein's anomaly was made in this case: a tendency to paroxysmal tachycardia, in association with a globular heart showing a prominent right border, systolic and diastolic murmurs with a triple rhythm and the electrocardiographic features of type B Wolff-Parkinson-White syndrome or, as was first the case, alternation with incomplete right bundle branch block. The absence of pulmonary plethora and hilar pulsations was good evidence against an atrial septal defect. No reasonable alternative diagnosis appeared likely. Further investigations in order to confirm the diagnosis were not made as the child was well and surgery not required.

Case 9

This 26-year-old bank clerk was referred because of discomfort in either side of the chest during the previous year; this was associated with emotional tension and not with exertion. On interrogation, he admitted that, for the last year or so, he had occasionally suffered from palpitations at rest. These consisted of the sudden onset of rapid regular heart-beats of 5-10 seconds duration which ended as quickly as they began. Their occurrence was quite erratic, sometimes two or three times in one day, and then not for many days. There were no significant illnesses in the past, the family history was normal, and he neither drank nor smoked. He was not taking any medication.

Examination revealed a healthy-looking and slightly obese young man (height 5'6"; 176 lb). The pulses were equal and not delayed, and the jugular venous pressure was not raised. The lungs were clear and he had no oedema. The heart was not enlarged clinically and the apex could not be palpated. The normal first and second heart sounds were heard without any murmurs. The remainder of the physical examination was entirely negative. His blood pressure was 130/80 mm.Hg.

Investigations revealed that urine, full blood count and the sedimentation rate were normal. The chest x-ray was normal, revealing no lung disease or evidence of cardiac enlargement or alteration in the cardiac contour.

Case 10

A 25-year-old farmer who had never had any symptoms of ill-health underwent life assurance examination which included an electrocardiogram and was rejected because of "atypical bundle branch block." He was referred for further assessment and denied any symptoms of ill-health in the past apart from childhood ailments and an attack of malaria at the age of 15. He denied episodes of palpitations.

Physical examination revealed him to be 5'10" tall and to weigh 195 lb. His pulse rate was 70 beats a minute and his blood pressure 130/80 mm. Hg. There were no abnormalities in the cardiovascular or other systems and urinalysis was negative. Chest x-ray was normal.

Case 11

Over a period of four years this 40-year-old man has suffered from several attacks of central chest tightness and breathlessness with palpitations, never lasting more than two or three hours. When admitted to hospital with similar symptoms, an electrocardiogram showed paroxysmal supraventricular tachycardia (Figure 48) which reverted to the Wolff-Parkinson-White syndrome with verapamil (Figure 63); the basic patterns in sinus rhythm are shown in Figures 25 and 26. Investigations have revealed no other abnormalities.

Case 12

This 62-year-old woman was referred to hospital complaining that for one year she had suffered from attacks in which she felt faint, and the heart pounded regularly: she tapped out a rate of over 200 beats per minute. The average duration of the palpitations was about 15 minutes. At first they occurred about once a month; but more recently they had occurred once in every one to three days. With them she had to sit down quietly. Immediately after an attack she felt the need to pass urine.

For some 30 years she had suffered from bronchitis during most winters, but was otherwise fit and suffered no dyspnoea on exertion. There was no history of premature heart disease and no members of the family were known to have suffered from palpitations. She smoked 5-6 cigarettes a day, but took no alcohol.

On examination she was seen to be anxious, but not pale; there was no tremor. The pulse rate was 80 beats a minute and the rhythm was regular. The blood pressure was 120/80 mm. Hg. The heart sounds were normal, with no added sounds or murmurs, and there were no signs of cardiac failure. Occasional rhonchi were heard in the chest, but the alimentary and nervous systems were normal. The urine, full blood count, sedimentation rate, serum transaminases, cholesterol, urea, electrolytes and glucose were normal. X-ray of the chest showed no cardiac enlargement or pulmonary disease.

Case 13

This 31-year-old West African (Ibo) male was admitted as an emergency. Six weeks previously he had suffered from palpitations and dyspnoea while playing table tennis. There had been a similar episode one week prior to admission. On the evening prior to admission he developed irregular palpitations and dyspnoea. There was no history of previous cardiac disorder. He had come to England six years previously, and worked as a civil service clerk; he was athletic. He had eaten a normal English diet. His parents had died when he was very young, the cause being unknown. His only brother was alive and well. His wife suffered from rheumatic heart disease. He smoked 20 cigarettes a day and consumed alcohol occasionally. There were no other relevant symptoms.

On examination he was mildly uncomfortable; there was no pallor, jaundice, cyanosis, clubbing or oedema or dyspnoea. His pulse rate was 64 beats a minute and irregular and his blood pressure was 85/55. The heart sounds were heard normally and he was thought to have an occasional third heart sound. The jugular venous pressure was not raised and the peripheral pulses were good; he did not have a pleural or pericardial friction rub. The respiratory, alimentary and nervous systems were normal.

The haemoglobin was 14.0 grams/100 ml. and the white blood count 4,800 per cubic mm. with neutrophils 56%, eosinophils 5%, basophils 1%, lymphocytes 33%, monocytes 4%. The sedimentation rate was 2 mm. in the first hour (Westergren), and the sickling test was positive. Electrophoresis of the haemoglobin showed the presence of haemoglobin A and S (sickle cell trait). The blood urea was 38 mg./100 ml., CO_2 24.5 mEq./l., potassium 4.0 mEq./l, sodium 132 mEq./l., fasting blood glucose 88 mg./100 ml. and cholesterol 117 mg./100 ml. (all normal) but there was elevation of the serum alanine transaminase (73 units), serum aspartate transaminase (73 units) and plasma lactic dehydrogenase 175 units (respective upper limits of normal of these are 40, 40 and 125).

A diagnosis of myocardial infarction was entertained. When seen in consultation next day, his blood pressure was 85/60 mm. Hg and the pulse 90 beats per minute with an irregular rhythm (Figures 71 and 72). Several hours later an alarm was registered on the cardiac monitor, and "ventricular tachycardia" was diagnosed by the duty registrar; within five minutes complete asystole had developed, and he failed to respond to external cardiac massage, intracardiac adrenaline, intravenous sodium bicarbonate, and direct current cardioversion.

A post mortem examination was carried out by Dr. D.A.L. Bowen, who reported that the body was that of a well built muscular Coloured person. The skeletal system was normal showing no evidence of bony injury.

Central nervous system: the cerebral vessels were congested and free of atheroma. The substance of the brain showed some congestion.

Cardiovascular system: the pericardial sac was healthy. The right ventricle was dilated and the wall 0.5 cm. thick; the left ventricle was 2 cm. thick. There was no valvular disease. There were a number of very tiny lipid plaques along the entire aorta. The right coronary artery was quite patent and healthy with no lipid plaques. The left coronary artery showed isolated plaques at the origin of the main descending artery and at one or two points at the bifurcation of the descending branches, but certainly no gross stenosis or occlusions. The myocardium was oedematous to the naked eye, and there were small localized fibrotic scars chiefly at the junction of the septum and posterior wall with some suggestion of more recent damage anteriorly.

Respiratory system: pleural sacs were dry and free of adhesions. Both lungs were intensely congested with some oedematous indurations.

Intestinal system: Quite marked congestion and oedema of the mucosal sacs of the stomach, with a little fluid present in the peritoneal cavity. There was post-mortem autolysis of the pancreas. The liver was intensely congested. The gall bladder was healthy.

Genito-urinary system: Both kidneys were of normal size and congested appearance. Vessels were normal and the bladder and prostate were normal.

Spleen: Firm, deeply-congested, weighing 355 grams.

The heart was then further examined by Professor R.E.B. Hudson at the National Heart Hospital, according to the technique described by him (Hudson, 1963).

Conducting System

Sinoatrial node: 16 pairs of sections were stained with haemotoxylin and eosin, and Van Gieson, taken at 2 mm. intervals. The anatomy is normal. The arteries are widely patent, possibly with some increase in fibrous interstitium.

Atrioventricular system: Serial sections were out at 6 u, every 15th section stained with Masson's trichrome (approximately 8 sections per mm.) Total number of sections: 300. Total distance examined: 3.7 cm. In addition 15 sections were taken at regular intervals throughout the series and stained with haemotoxylin and eosin.

Atrioventricular node - moderate replacement fibrosis, but is large and otherwise normal. Vessels normal.

Penetration - Normal. Focus of myocarditis in inferior margin of node.

Bundle of His - large, well-defined and running mainly on the left side of the upper limit of the interventricular septum. The muscle cells are small and separated by excess fibrous interstitium. Also there are scattered foci of myocarditis. (Some fasciculi can be seen to arise and almost to make contact with the interventricular septal muscle (Figure 89).

Left fascicles - the fascicles are attenuated and traverse large areas of subendocardial myocarditis.

Bifurcation - most of the major portion of the bundle remains on the left side. The right branch is small.

Right branch - remains small and intramyocardial throughout its course. In many places it becomes ill-defined from fibrosis or from involvement in myocarditis. In several places it is not possible to distinguish it from nearby myocardium.

PAS staining of bundle of His shows no Gee's glycoprotein masses.

Summary - active non-specific subacute myocarditis chiefly in the interventricular septum and involving parts of the bundle of His and both branches. Although the histological anatomy is normal the degree of damage to the branches could account for dysrhythmia in life. No accessory pathway identified in the area examined. The myocardium proper showed widespread non-specific subacute myocarditis (Figures [illegible] and [illegible]) such as could be associated with almost any infective illness - viral, bacterial, rickettsial or protozoal.

At the stage at which the patient was seen he was too ill to give a good account of himself. There was nothing to suggest myocardial infarction, although he did indicate that he had suffered from chest pains that he defined with difficulty. Whether or not he had ventricular tachycardia or fibrillation terminally it is impossible to say; this impression was drawn from the cardioscope. It was in the firm expectation that an abnormal pathway could be demonstrated that Professor Hudson was asked to examine the heart in detail. He found a most intense myocarditis, but there were no signs of an anomalous tract actually connecting the atria, the bundle of His or the bundle branches to the myocardium (for discussion, see Chapter 12).

Figure 89 (Case 13) Fasciculi arising from bundle of His (right) are seen in centre of picture: they do not reach interventricular septal muscle (left). (Masson's trichrome, low power).

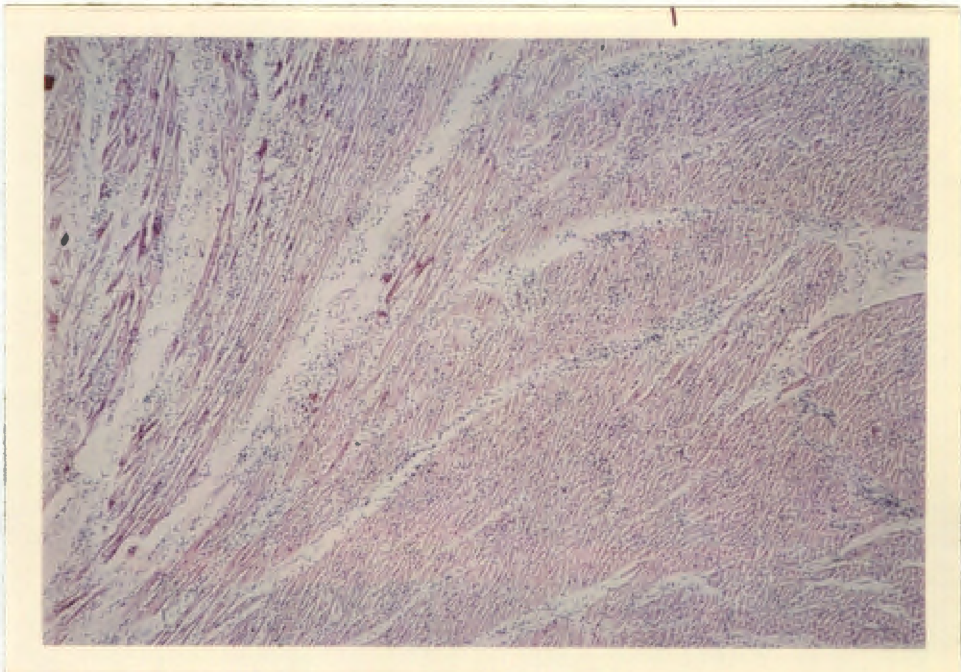


Figure 90 (Case 13) Myocardium (low power) (H. and E.).

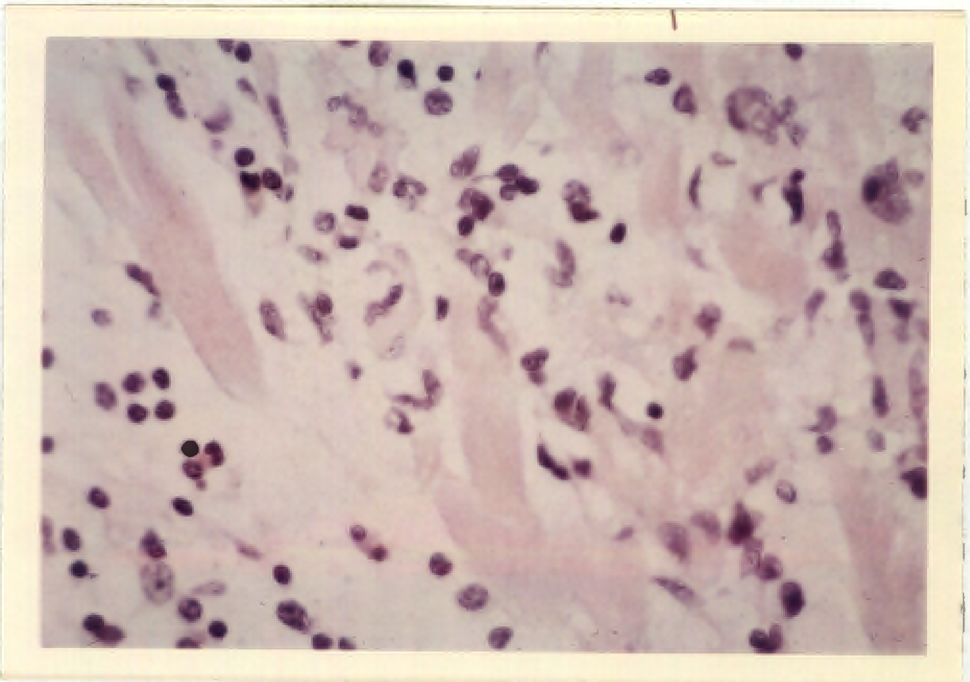


Figure 91 (Case 13) Myocardium (high power) (H. and E.).

Case 14

This 53-year-old male book-keeper had for at least 10 years suffered from occasional attacks of faintness, associated with awareness of cardiac action, usually under conditions of emotional stress. While in the bus on the way to work he felt faint, with the characteristic anxiety and sweatiness that he had previously suffered, and this continued for several minutes. A bystander brought him to hospital, and he was admitted for observation. There were no significant features in the past or family history. He smoked 20 cigarettes per day and his consumption of alcohol was moderate.

The patient was not in cardiac failure, and had a pulse rate of 68 beats a minute, with a blood pressure of 180/90 mm. Hg. The heart was not enlarged clinically, and the heart sounds were normal without added sounds or murmurs. The respiratory, alimentary and nervous systems were likewise normal. Full blood count, sedimentation rate, blood urea, electrolytes and transaminases, and a chest x-ray were all normal. An electrocardiogram was normal before (Figure 67) and after effort.

It was considered that time that the patient had not suffered from cardiac infarction, but it was suspected that there had been some cardiac ischaemia associated with paroxysmal tachycardia, possibly due to the Lown-Ganong-Levine syndrome. Eight days after admission, he was noticed to become unconscious while being examined. An electrocardiograph was recorded immediately and the appearances seen in Figure 68 noted: ventricular fibrillation was diagnosed. Direct current defibrillation was applied using a charge of 80 joules and 300 ml. of 8.4% sodium bicarbonate given by intravenous infusion. There was immediate conversion of the rhythm, and the ensuing arrhythmias are shown in Figure 68 and discussed in Chapter 11. Intravenous lignocaine was administered when ventricular tachycardia developed (Figure 68d). The patient remained unconscious for 30 minutes and was confused for another 36 hours, after which he returned to his previous state. On the day after the event the serum aspartate transaminase had risen to 58 units, the alanine transaminase to 48 units, and the lactate dehydrogenase to 115 units.

The patient gives a history compatible with a paroxysmal arrhythmia of very brief duration, episodes usually lasting no more than a minute each, with the exception of an attack of palpitations with chest discomfort on the day of admission. An alert resident considered the possibility of pre-excitation on the basis of a borderline P-R interval noted on the initial electrocardiogram (Figure 67); this was subsequently seen in another five tracings taken during his stay in hospital. It was considered that the normal enzyme estimations excluded myocardial damage resulting from an infarct and the lack of abnormality in an electrocardiogram recorded after exertion was taken as evidence against the presence of ischaemic heart disease. Quite spontaneously, he developed ventricular fibrillation while in hospital, and this was fortuitously noticed within moments of its onset. No precipitating factor leading to this was identified, and he did not appear to have suffered a significant cardiac infarct, as several follow-up electrocardiograms were practically unchanged once the initial T wave inversion following the arrhythmia had returned to normal after two hours. The enzyme changes were mild and considered to represent cardiac ischaemia resulting from the ventricular fibrillation, as well as muscle damage caused by the cardioversion. Reasons for postulating an anomalous bypass in this case are discussed in Chapter 11.

Case 15

A 12-year-old boy was referred because of the discovery of a soft systolic murmur. His effort tolerance was good, the murmur was considered to be an innocent pulmonary ejection systolic bruit, and there were no other clinical abnormalities. An x-ray of the chest and full blood count were normal, and he was not considered to have cardiac disease; a short P-R interval was the sole untoward finding on the electrocardiogram (Figure 39). There was no history to suggest an arrhythmia.

Case 16

This 62-year-old man was admitted to hospital having suddenly lost consciousness at home (Garrett and Krikler, 1972). He was mildly confused but alert when examined, and able to give a full account of himself the following day. He had left school at the age of 14, and had worked as a labourer in the building trade since 1936. In 1941 he joined the Royal Navy and was passed A1 on entry as well as on discharge in 1945. Several months later he had the first of his blackouts. These have always followed the same pattern, and tend to occur at irregular intervals, perhaps every three or four weeks: the heart suddenly speeds up, things look yellow and, if standing he suddenly loses consciousness, falling to the floor, and recovering within a minute or two. He has never been seen to have jactitations. On other occasions he might have the sudden palpitations while sitting or lying; then he would not lose consciousness; they would last up to 20 minutes, and disappear suddenly. During them he would feel unable to move, but denied dyspnoea or chest pain. He was informed in 1945, after the first attack, that his right pupil was dilated, and had been aware of this since.

Although these attacks continued he was not admitted to hospital or investigated until 1960, when, while walking to work, he suffered a typical "blackout" preceded by sudden regular palpitations. Unconsciousness lasted 10 minutes only, and the only physical abnormality recorded in the hospital notes was of dilatation of the right pupil; the fundi were normal. His blood pressure was 110/80 mm. Hg, the pulse was regular (80 beats a minute), and a lumbar puncture produced hazy cerebrospinal fluid at "normal pressure;" the protein was 85 mg/100 ml., sugar 90 mg./100 ml., and there were 173 white cells per cubic mm. of which 5% were neutrophils and 95% lymphocytes, with a chloride of 700 mg./100 ml. The Wassermann reaction was positive and the Lange curve was considered to be paretic: 3322220000. The patient remained well and was discharged, but did not reattend, and no treatment for syphilis was given.

In 1963 he was referred because of persistent fainting attacks. Normal results were obtained for a full blood count, sedimentation rate, blood urea, electrolytes, glucose, proteins and acid and alkaline phosphatases. The urine was chemically and microscopically normal and sterile. X-rays of the chest and skull were normal, with no evidence of calcification of the root of the aorta or of widening of the aortic arch. Serological tests for syphilis on the blood showed that the Reiter protein complement fixation test was weakly positive; the V.D.R.L. slide test was positive with the serum diluted 1 in 8; the cardiolipin Wassermann reaction was positive; and the fluorescent treponemal antibody test was positive. A lumbar puncture was performed and clear colourless fluid was obtained at a pressure of 120 mm. of C.S.F. This contained protein 25 mg./100 ml., no excess of globulin, glucose 68 mg./100 ml; and fewer than three white cells per cubic mm. The following serological tests were performed on the C.S.F., and were all negative: Reiter protein complement fixation test; V.D.R.L. slide test, and cardiolipin Wassermann reaction. Thereafter he was periodically depressed, tended to gamble, and suffered from sleeplessness. In 1967 he attempted to kill himself by gassing, but recovered rapidly:

the cerebrospinal fluid was found to contain protein 45 mg./100 ml. with an increase in the globulin; lymphocytes 25 per cubic mm.; Wassermann reaction positive. A course of procaine penicillin (600,000 units daily) was given for ten days. Since then he has complained of stabbing pains in the legs, in addition to the other symptoms; his behaviour pattern has remained unchanged.

The patient was mildly disorientated, and clearly facile. The pulse was 80, and regular, and the peripheral pulses were all normally palpable. His blood pressure was 130/90 mm. Hg. The heart was not enlarged clinically and there were no cardiovascular abnormalities. The respiratory and alimentary systems were also normal. In the central nervous system, the sole cranial nerve abnormalities consisted of dilatation of the right pupil with both pupils failing to react to light, but responding normally to convergence. There was no ptosis, but he was mildly dysarthric. Co-ordination was sound in both upper and lower limbs and there was no loss of power. Both ankle jerks were absent, but the knee reflexes and the upper limb reflexes were intact; the plantar responses were flexor.

Superficial pain sensation and vibration sense were absent below the knees, but proprioception was normal and Romberg's test was negative.

The clinical diagnosis of tabes dorsalis was made and it was felt that the personality disorder and mild dysarthria suggested that he in addition suffered from some signs of general paralysis, i.e. taboparesis. An electroencephalogram showed a low voltage alpha rhythm of 8-9 cycles per second in the post-central areas, which blocked to eye opening. Minimal theta activity was scattered through the record. Overbreathing added no further information. Symmetrical following responses were evoked by rhythmic photic stimulation. The electroencephalogram was pronounced to be within normal limits. A further course of procaine penicillin, 600,000 units intramuscularly daily, was given for 15 days.

During his stay in hospital, he had three attacks of palpitations. On one occasion he was lying in bed, and the attack persisted for 30 minutes before it disappeared spontaneously while an electrocardiogram was recorded which revealed it to be atrial flutter with 2:1 block, producing ventricular rate of 160 beats per minute (Figure 56). On the next occasion he was also in bed, but stood up and lost consciousness; he was returned to bed and was found to have a regular tachycardia (140 beats a minute), with a blood pressure of 80/60 mm. Hg. Verapamil was administered by intravenous injection in the dose of 10 mgm. over a 15 second period, and after 136 seconds this was converted to sinus rhythm (Figure 64). A third attack was subsequently observed and treated in the same way.

Case 17

This 58-year-old man has suffered from paroxysmal supraventricular tachycardia for 2½ years. This had first been noticed during a febrile illness considered to be myocarditis of possible viral etiology. He was quite well apart from the fact that he had been suffering from attacks of paroxysmal supraventricular tachycardia which reduced his exercise tolerance. The clinical features have been published by Reckless and Gilchrist (1971), and there are no other abnormalities present.

<u>Case 18</u>

This 61-year-old man has suffered from paroxysms of rapid irregular palpitations for 7 years. On several occasions he had been admitted to another hospital, where atrial fibrillation had been identified. He had been treated with digoxin, propranolol, practolol and quinidine in varying combinations, but attacks continued, lasting between three minutes and two hours at a time. With the more severe and prolonged attacks he had dyspnoea and vague chest discomfort. At no stage had electrocardiograms revealed evidence of cardiac infarction. He was kept on maintenance digitalis. There was no significant past history. He occasionally smoked cigars but drank no alcohol.

On examination he had a pulse rate of 160 beats a minute, and the rhythm was totally irregular. The cardiac apex was not palpable, and no abnormal sounds were heard. There were no signs of cardiac failure. His blood pressure was 150/80 mm. Hg. The attack ended spontaneously after he had been in the ward for 30 minutes. Six further attacks occurred during the next ten days; they were all short-lived, rarely exceeding 30 minutes in duration. The attacks have continued despite the administration of digoxin, propranolol, practolol, quinidine and phenobarbitone, and he was readmitted several times on this account.

Normal results were repeatedly obtained for all investigations, including: full blood count, sedimentation rate, serum proteins, lipids, electrolytes, urea, protein-bound iodine and resin uptake of triiodothyronine. A x-ray of the chest was normal, with a cardiothoracic ratio of 48%, no left atrial enlargement, normal cardiac pulsations on screening, and clear, non-emphysematous, lung fields. On clinical grounds and after investigation it was thus felt that rheumatic, ischaemic and hypertensive heart disease, thyrotoxicosis, atrial septal defect, chronic cor pulmonale, constrictive pericarditis and intracardiac tumours could be excluded and lone atrial fibrillation be diagnosed.

Case 19

A 22-year-old woman presented with rapid regular palpitations (of three hours duration) for the twelfth time in seven years; these attacks were never disabling. She was not in cardiac failure; the heart rate was 160 beats a minute and the blood pressure 110/70 mm. Hg; there were no other abnormalities. The arrhythmia failed to respond to carotid sinus pressure but she reverted to sinus rhythm after intravenous verapamil. No cardiac or other abnormalities were then evident, x-ray of the chest and a full blood count being normal also. One further attack, also responding to verapamil, occurred four months later.

Case 20

This 50-year-old taxi-driver had suffered from mild, well-controlled diabetes mellitus for six years, and had suffered from cardiac infarction four years previously. He presented with the acute onset of rapid regular palpitations and dyspnoea, but no chest pain. His blood pressure was 120/70 mm. Hg and the heart rate 170 beats a minute. Fine crepitations were heard in both lung fields, but there were no other signs of cardiac failure. The heart sounds were normal. The tachycardia failed to respond to carotid sinus pressure but reverted to sinus rhythm after intravenous verapamil. In sinus rhythm, there were no abnormalities in the cardio-vascular system, and the electrocardiogram revealed no relic of the old cardiac infarct.

Full blood count, sedimentation rate, serum trans-aminases and lipids and blood urea and electrolytes were normal, and x-ray of the chest revealed clear lung fields and a normal cardiac contour. The fasting blood glucose, initially 145 mg./100 ml., has been kept at or below 110 mg./100ml. with dietary control.

Case 21

This 48-year-old Jamaican housewife has lived in England for ten years. She had been quite well until four years previously when she found to be mildly hypertensive and for this she had intermittently received treatment with diuretics. For three years she has experienced attacks of palpitations associated with faintness, coldness and sweatiness. In one attack she was admitted elsewhere, and her pulse was found to be irregular, at the rate of about 150 beats per minute; the blood pressure was 160/90 mm. Hg. There were no signs of cardiac failure. No cardiac murmurs were heard, atrial fibrillation was found on electrocardiogram, and the patient was admitted to hospital. The hospital summary indicated "there was no evidence of myocardial infarction either on the electrocardiograms or blood enzyme tests." Sinus rhythm returned spontaneously. Chest x-ray showed considerable cardiac enlargement and she was thought to have a cardiomyopathy. A large number of investigations were all negative; these included the haemoglobin, sedimentation rate, blood urea and electrolytes, liver function tests, electrophoresis of the serum proteins, examination of the peripheral blood for lupus erythematosus cells, sickle cell test, electrophoresis of the haemoglobin, an intravenous pyelogram and biopsy of gum and rectal mucosa stained with Congo red for amyloid.

Several further attacks of palpitations occurred, and practolol was added. Despite this, she continued to be troubled, and stopped all therapy. Three weeks later she was admitted with paroxysmal tachycardia in which the cardiac rate was 150 beats per minute and the rhythm was regular. The blood pressure was 130/80 mm. Hg, the lungs were clear, the neck veins were not distended and there was no oedema. The first and second heart sounds were heard with no murmurs or additional sounds. The alimentary and nervous systems were normal and urinalysis was negative.

Intravenous verapamil produced atrial fibrillation; cardioversion (50 joules) then restored sinus rhythm. Attacks of paroxysmal tachycardia subsequently responded to verapamil or cardioversion; for several months, while taking verapamil 40 mg. four times a day by mouth, she has had no further attacks.

In sinus rhythm she has a forceful left ventricular apical impulse and a loud fourth heart sound. Further investigations have all proved negative but there is marked cardiomegaly on x-ray. On moderate doses of methyldopa (750 mg. daily) and bendrofluazide (5 mg. daily) her blood pressure averages 155/95 mm. Hg.

It seems reasonable to make the diagnosis of congestive cardiomyopathy here. The hypertension is relatively mild, and the cardiac enlargement gross; only during paroxysmal arrhythmias does left ventricular failure become clinically evident. No other general diseases were discovered despite thorough investigation.

Case 22

This 59-year-old carpenter had moved to England from Jamaica fifteen years previously, in 1956, and had been well (except for an attack of pneumonia in 1957) until the onset of the present illness. According to the x-ray report in 1957 the heart size was not increased at that time. He was admitted to hospital complaining of progressive dysponea on exertion for three years, and orthopnoea, paroxysmal nocturnal dyspnoea and oedema of the ankles for four weeks.

Examination revealed the patient to be in congestive cardiac failure, with elevation of the jugular venous pressure to 3 cm., sacral and ankle oedema, and bilateral basal crepitations. There was no evidence of cardiac enlargement clinically, and no murmurs were heard; there was a moderate fourth heart sound. The pulse was totally irregular (rate about 60 beats a minute) and the blood pressure 170/100 mm. Hg, with no pulsus paradoxus. The liver edge was palpable 3 cm. below the right costal margin. The remainder of the physical examination was normal. Full blood count, sedimentation rate, blood urea, electrolytes and proteins were normal. X-ray of the chest showed pulmonary congestion and moderate cardiac enlargement (cardiothoracic ratio 54%) with slightly diminished pulsations of the left ventricle on screening.

His cardiac failure responded rapidly to bed rest, digoxin and bendrofluazide, but the digoxin was stopped after 4 days because the pulse rate fell to 40 beats a minute and he became nauseated; the bendrofluazide was continued. The lungs were radiologically as well as clinically clear of congestion within one week, and he lost the oedema and other evidence of cardiac failure.

On the basis of the mildness of his hypertension with gross left ventricular hypertrophy, and in the absence of valvular lesions or evidence of cardiac ischaemia or pericardial effusion, or alcoholism or other general diseases, congestive cardiomyopathy was diagnosed in this Jamaican patient.

Case 23

This 57-year-old woman was admitted because of sudden onset of dyspnoea. There had been five similar, albeit milder, episodes during the preceding four months, and she had also noticed that she was mildly short of breath on exertion, e.g. walking 400 yards. There had been no retrosternal tightness. No history of rheumatic fever or any other serious ailment could be obtained.

The patient was acutely dyspnoeic with widespread coarse crepitations and wheezes throughout both lung fields, and the production of small amounts of frothy pink-tinged sputum. The pulse rate was 100, and the rhythm was regular; the blood pressure was 150/90 mm. Hg. The jugular venous pressure was raised 4 cm. above the sternal angle but there was no dependent oedema and the liver was not enlarged. The heart did not appear enlarged clinically at that time, but a fourth heart sound could be heard from time to time; the first and second heart sounds were normal and a loud mitral systolic murmur, occupying the whole of the cycle, was most clearly audible at the cardiac apex, and conducted to the lower left sternal edge as well as just into the left axilla. No other physical abnormalities were noted.

The patient was obviously in left ventricular failure and this was confirmed radiologically by the finding of pulmonary oedema; the heart was moderately enlarged also. There was a prompt response to the intravenous injection of digoxin, frusemide and aminophylline; she had a marked diuresis and within 2 hours was comfortable.

Full blood count and sedimentation rate were normal. Serial measurements of the serum aspartate and alanine transaminases were normal. The blood urea was 56 mg./100 ml. on the day after admission and 44 mg./100ml., three weeks later; the serum electrolyte levels were all normal.

Two days after admission the patient had a further attack of pulmonary oedema which again responded to intravenous frusemide and aminophylline and was then given oral bendrofluazide 10 mg. each morning. On the fifth day in hospital atrial fibrillation was noted; this responded to verapamil (Figure 81) and she subsequently reverted to sinus rhythm within 24 hours. The patient was referred for cardiac catheterization which was carried out by Dr. Raphael Balcon; she was not then in cardiac failure. The data appear in Table XVIII.

These findings indicated that the left ventricular end-diastolic, pulmonary artery, and right ventricular systolic pressures were all elevated. No valve gradients were detected in the control state or after isoprenaline or ectopic beats.

Angiocardiography was then carried out. The left ventricular pictures showed a large cavity with apparently good contractility on the cine films. There was slight regurgitation into a small left atrium, and no filling defect was seen. Coronary angiography revealed that there was a dominant left circulation; there were no obstructive lesions seen in any vessels.

On the basis of the elevation of the left ventricular end-diastolic, pulmonary artery and right ventricular systolic pressures, and the absence of gradients, together with dilatation of the left ventricular cavity, minimal mitral regurgitation, and normal coronary arteries, it was concluded that the diagnosis was that of cardiomyopathy.

Table XVIII

Site	Pressure (mm.Hg Ref. Mid-Chest)	Time Elapsed Mean(Mins.)	O2 Oxygen Satn. (%)	Time Elapsed (Mins.)
Superior vena cava (Low)			69	63
Mid-right atrium		5	54	63
Inferior vena cava (High)			54	62
Right Ventricle (Body)	45; End-Diastolic = 5			
Main Pulmonary Artery	45/18	30	68	60
Pulmonary Artery (Wedged)	A=30, X=20, V=40, Y=20	30		
Left ventricular apex	250; End-Diastolic = 35			
Aorta	240/100	150	97	60

Table XVIII (Cont.)

Data for Flow Calculations

Flow measured by Fick principle
Oxygen Saturation measured by Oximetry
Oxygen Consumption - 168 c.c./Min./Sq.M. (Assumed Basal)
Haemoglobin = 11.9 G./100 ml.
Oxygen Capacity = 15.8 c.c./100c.c.

Calculations

Pulmonary Flow (QP)	=	2.3 L./Min./Sq.M.
Systemic Flow (QS)	=	2.3 L./Min./Sq.M.

Peak Gradient

Aortic Valve	10 mm. Hg
Pulmonary Valve	0 mm. Hg

Mean Gradient

Mitral Valve	0 mm. Hg
Tricuspid Valve	0 mm. Hg

The patient appears to suffer from congestive cardiomyopathy of unknown cause. She had been kept free of cardiac failure by maintenance treatment with digoxin and diuretics, and has had no recurrence of atrial fibrillation.

Case 24

This 54-year-old school teacher had settled in England from Jamaica in 1955, fourteen years before admission. He had been well until one week before admission, when he developed a feverish illness with cough and dyspnoea. Within four days the dyspnoea had become very much worse. The pulse rate was 100 beats a minute, and the rhythm was regular; there was clinical evidence of marked pulmonary congestion with numerous crepitations heard in both lungs, together with rhonchi and wheezes. The neck veins were not distended, the liver was not palpable and there was no oedema of the ankles or over the sacrum. The blood pressure was 130/80 mm. Hg, and the temperature 101°F. No other physical abnormalities could be found. The urine was normal. X-ray of the chest showed considerable congestion of both lung fields and marked cardiac enlargement; in addition, there was patchy consolidation at the right base. The haemoglobin was 15 G./100 ml., packed cell volume 50%, white blood count 4,300/cu.mm. and sedimentation rate 25 mm./hour (Westergren). The blood urea was 40 mg.100 ml.

The diagnosis of bronchopneumonia and cardiac failure was made, and he responded well to ampicillin, digoxin and frusemide. The patient had an intense diuresis and lost his dyspnoea by the third hospital day; both the consolidation and the pulmonary congestion had cleared radiologically, and the cardiac enlargement had decreased slightly, after 10 days.

It was quite impossible to be sure of the presence or absence of cardiac murmurs at the time of admission, but he has subsequently never exhibited any murmurs though a soft fourth heart sound was audible.

The patient was seen on a number of occasions in the out-patient clinic, and it was confirmed that his consumption of alcohol was moderate. He has been able to return to normal work, with no restriction of activity.

This appears to be another patient with idiopathic congestive cardiomyopathy, previously and subsequently asymptomatic, although cardiac failure was precipitated by bronchopneuemonia.

Case 25

This 76-year-old man was first seen three years previously for transient right hemiparesis. He was found to have cardiac enlargement, no signs of cardiac failure, a blood pressure of 170/70 mm. Hg, and the signs of aortic incompetence and mitral stenosis and incompetence. He had suffered from rheumatic fever on three occasions during childhood, but had been able to work as a sales assistant until he retired at the age of 65. Digoxin was started one year after the stroke because of dyspnoea.

Investigations have all been normal apart from moderate cardiomegaly on x-ray, with a cardiothoracic ratio of 56%, and signs indicative of left ventricular and atrial enlargement and aortic unfolding.

Case 26

This 83-year-old man was referred because of occasional mild angine pectoris on exertion. He was not taking digitalis. He suffered from carcinoma of the prostate as judged by rectal examination; there were no mestastases. The pulse was slightly irregular due to occasional extrasystoles, and the blood pressure was 180/90 mm. Hg. The heart was slightly enlarged clinically, and there was a grade 3/6 aortic ejection systolic murmur. The remainder of the examination was negative and the urine was normal. Full blood count, sedimentation rate and serum alkaline and acid phosphatase were normal; the blood urea was 56 mg./100 ml. X-ray of the chest showed slight ventricular enlargement (cardiothoracic rate 52%).

Case 27

The patient, now aged 62, is a business executive who had suffered a severe anterior cardiac infarct 16 years previously. Review of his notes indicates that he had experienced transient hypotension then, and that the serum aspartate transaminase had been elevated. He made a slow but almost complete recovery, experiencing angina only on severe effort. His electrocardiograms were available for review and have developed the present pattern (Figure 87) gradually: it has been established for 10 years, though precise comparison is difficult because of the poor characteristics of the machines previously used (Krikler, 1971b).

The patient has been seen on several occasions and the findings and investigations have revealed similar results. He is a short moderately-obese man, 5'4" in height, who weighs 156 lb. His blood pressure is 140/80 mm. Hg. There are no other clinical abnormalities.

Investigations have revealed slight cardiac enlargement on chest x-ray, with a cardiothoracic ratio of 52%; on screening there was no evidence of a cardiac aneurysm. The serum cholesterol was 330 mg./100 ml. and triglycerides 112 mg./100 ml; electrophoresis showed elevation of the betalipoprotein.

Perspectives

The pre-excitation syndromes impinge on so many aspects of cardiology that they are important beyond their relative infrequency. In the first place, their understanding demands the logical interpretation of the information currently available by clinical, electrophysiological and anatomical methods of study. Even so - as will be apparent from the foregoing - we as yet know too little about them. In this work, some of the open questions have made themselves apparent, and further analysis of data along the lines indicated is essential. A registry of patients will be useful in their careful follow-up so that the gaps in our knowledge of their natural history can be filled. Interchange of information between centres where they are studied in depth is basic to further advances. Pre-excitation can be looked upon as a model where the understanding of the mechanisms of more general problems of arrhythmias and conduction disturbances can be pursued. The limited contribution provided by the present thesis owes much to the stimulus and cooperation of others, and it is only together with them that further work can prove fruitful.

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